

BIOLOGIA MOLECULAR

Martins MV, Lima MC, Duppre NC, Matos HJ, Spencer JS, Brennan PJ, Sarno EM, Fonseca L, Pereira GM, Pessolani MC. The level of PPD-specific IFN-gamma-producing CD4+ T cells in the blood predicts the in vivo response to PPD. *Tuberculosis* 2007; 87(3): 202-11.

There are no reliable means for detecting subclinical mycobacterial infections. The recent sequencing of several mycobacterial genomes has now afforded new opportunities for the development of pathogen-specific diagnostic tests, critical in the context of leprosy and tuberculosis control. In the present study, we applied a multi-parametric flow cytometric analysis that allowed the investigation of T-cell functions in order to define immunological markers that measure previous exposure to mycobacteria. We compared the in vivo response to PPD, the gold standard skin test reagent for measuring previous exposure to *Mycobacterium tuberculosis*, with in vitro parameters of leukocyte activation in five PPD positive and five PPD negative healthy volunteers. PPD-stimulated peripheral leukocytes expressing CD4, CD69, cutaneous lymphocyte-associated antigen (CLA) and intracellular IFN-gamma were enumerated in whole blood and compared with the size of in vivo PPD-induced induration and IFN-gamma production levels as measured by ELISA in supernatants of PPD-stimulated peripheral blood mononuclear cells. The reactivity to the tuberculin skin test (TST) was associated with markedly increased frequencies of PPD-responsive activated (CD69+) and IFN-gamma-producing CD4+T cells. Detection of PPD-specific IFN-gamma producing leukocytes was restricted to CD4+T cells and a subset of these cells was shown to express the skin homing molecule CLA. Multiple linear regression modeling of responses to PPD showed the highest association between skin test indurations and frequencies of PPD-responsive IFN-gamma-producing CD4+CD69+ T cells. Our data show that the in vitro enumeration of antigen-specific IFN-gamma-producing CD4+ T cells can provide an alternative to the in vivo tuberculin test for the detection of latent *Mycobacterium tuberculosis* infection. Moreover, the measurement

of these immunological parameters can be useful for the screening of new specific antigens defined by the genome sequence allowing selection of the best candidates for new diagnostics (including new skin tests), and vaccines for leprosy and tuberculosis.

Sapkota BR, Ranjit C, Macdonald M. Rapid differentiation of *Mycobacterium tuberculosis* and *Mycobacterium leprae* from sputum by polymerase chain reaction. *Nepal Med Coll* 2007 J; 9(1): 12-6.

Differentiation of *M tuberculosis* and *M leprae* by polymerase chain reaction (PCR), when acid-fast bacilli (AFB) were present in sputum from patients at Anandaban hospital, was carried out. Thirty sputum samples microscopy positive for AFB were collected and were subjected to culture. Bacterial DNA was extracted and PCR was performed using primers specific for *Mycobacterium tuberculosis* and *Mycobacterium leprae* DNA. Twenty samples were from patients with clinical TB and 10 from patients with clinical leprosy. Fifteen of the TB samples were positive in both TB PCR and culture, among the reminders four were TB PCR negative and one was positive for TB PCR. All TB samples were negative for leprosy PCR. Of the leprosy samples, five were TB PCR and culture positive, and negative for leprosy PCR. The remaining five samples were negative for both TB PCR and culture but positive in leprosy PCR. Five often clinical leprosy samples were positive for tuberculosis. This indicates that AFB in the sputum of leprosy patients might be *M. tuberculosis* or *M. leprae*. Thus PCR can be used for rapid differentiation of *M. tuberculosis* and *M. leprae* present in sputum where AFB microscopy is inconclusive.

CLÍNICA

Nishida M, Nakamura Y, Aosaki N. Título: [Elderly depression in a Japanese leprosarium]. *Nihon Hansenbyo Gakkai Zasshi* 2007; 76(1): 3-9.

This report described the distribution of the patients who had been treated by psychiatrist in the National Tamazenshouen Sanatorium, a major leprosarium in Japan. We also investigated the characteristics of patients who had suffered a depressive episode during the last 5 years. Somatic symptoms were the predominant symptoms and were not limited to clinical signs unique to leprosy. The period of isolation was not significantly correlated with the geriatric depression scale. Forty-two residents had committed suicide since the leprosarium was established in 1909. The findings of this study emphasize the importance of psychosocial intervention to the residents.

Böddinghaus BK, Ludwig RJ, Kaufmann R, Enzensberger R, Gies V, Kramme S, Brade V, Brandt CM. Leprosy in a pregnant woman. *Infection* 2007; 35(1): 37-9.

Herein, we describe a case of leprosy in a 29-year-old pregnant southeast-asian woman who presented with joint pain and multiple disseminated erythematous macules, papules and plaques. Histological examination and stains for acid-fast bacilli from skin biopsies substantiated the clinical suspicion of a cutaneous mycobacterial disease and both should be performed in all patients with unidentified skin lesions. The definitive laboratory diagnosis of leprosy was achieved by the application of a species-specific real-time polymerase chain reaction from infected tissue.

Santos DO, Castro HC, Bourguignon SC, Bastos OM, Rodrigues CR, Van Heuverswyn H, Nery JA, Miranda A. Expression of B7-1 costimulatory molecules in patients with multibacillary leprosy and reactional states. *Clin Exp Dermatol* 2007; 32(1): 75-80.

BACKGROUND: The expression of B7 as a costimulatory molecule on the surface of antigen-presenting cells such as macrophages and on dendritic cells characterizes the efficiency of the cell-mediated immune response. **AIMS:** Our purpose was to evaluate B7-1 expression in peripheral blood mononuclear cells (PBMCs) immediately after cell isolation ('spontaneous' B7 expression), and in inflammatory cells from cutaneous lesions of patients with multibacillary leprosy (MB-L) without and during the reactional states of erythema nodosum leprosum (ENL) or reversal reaction (RR). **METHODS:** Peripheral blood samples and skin biopsies of eight patients without (MB-L) and with reactional episodes (ENL and RR) were studied using antibodies against B7-1, CD1b, DR and CD14 in flow-cytometry and immunohistochemistry experiments. **RESULTS:** The flow-cytometry studies (mean +/- SD% of fluorescent cells) revealed significant B7-1 expression on PBMCs isolated from patients with ENL (8.0 +/- 0.6%) and RR (15.0 +/- 1.4%) compared with that observed for patients with MB-L (0.4 +/- 0.2%). Similar results were observed for cutaneous lesions of these patients by immunohistochemical assays. One patient studied before and during ENL revealed weak B7 expression before the reactional episode (0.3% of cells) compared with the marked level of B7-expressing cells detected during ENL (8.5% fluorescent cells). Interestingly, an even higher B7 expression (15% of cells) was observed in patients with RR. **CONCLUSIONS:** Our results strongly suggest that B7 expression precedes reactional episodes in MB-L, which could be related to the acquisition of effective immunity to *Mycobacterium leprae* during reactional episodes in leprosy. We propose B7 expression as a marker of CMI response in reactional episodes in leprosy.

Husain S, Malaviya GN. Early nerve damage in leprosy: an electrophysiological study of ulnar and median nerves in patients with and without clinical neural deficits. *Neurol India* 2007; 55(1): 22-6.

BACKGROUND: Peripheral nerve trunk involvement in leprosy is very common. However, by the time it becomes clinically manifest, the damage is quite advanced. If the preclinical nerve damage can be detected early, the deformities and disabilities can be prevented to a large extent. **AIMS:** To assess the electrophysiological functions of the ulnar and median nerve trunks in cases of clinically manifest leprosy with and without manifest nerve damage at different durations of nerve damage. **MATERIALS AND METHODS:** Electrophysiological functions of ulnar and median nerves were studied in leprosy patients, both normal and at different stages of disease and damage. PB cases, having disease for six months or less, without neurological symptoms and clinically normal appearing nerve. **STATISTICAL METHODS:** Mean was taken of different values. The changes in values of different parameters were expressed as percentage change with reference to the control values (increase or decrease). **RESULTS:** Reduced nerve conduction velocities and changes in latency and amplitude were observed. Changes in sensory nerve conduction were more pronounced. Sensory latencies and amplitude changes were more severe than motor latencies and amplitudes in cases with manifest muscle palsies. Changes in MB cases were less marked. **CONCLUSIONS:** Further studies are needed to identify parameters likely to be helpful in the diagnosis of early nerve damage.

Kiris A, Karlidag T, Kocakoc E, Bozgeyik Z, Sarsilmaz M. Paranasal sinus computed tomography findings in patients treated for lepromatous leprosy. *J Laryngol Otol* 2007; 121(1):15-8.

Nasal and paranasal sinus involvement is common in lepromatous leprosy and is of considerable epidemiological significance. The aim of this study was to investigate paranasal sinus abnormalities in treated lepromatous leprosy cases and to evaluate the findings in comparison with those of previous studies. **MATERIALS AND METHODS:** Thirty-eight patients who had been treated for lepromatous leprosy were included. All patients had been treated with dapsone and rifampicine for six months, and followed with dapsone, rifampicine and clofazimine for a minimum of two years. All patients received a clinical examination, a coronal computed tomography (CT) examination of the paranasal sinuses and ethmoidal sinus endoscopy, in order to investigate the involvement of the paranasal sinuses in the leprosy. Ethmoidal sinus biopsies were taken in 18 of the 21 cases of ethmoidal sinus involvement noted on CT scan. **RESULTS:** Twenty-three patients had sino-nasal symptoms. Endoscopic examination showed different pathologies in 21 of these patients. Abnormalities in the paranasal CT images were observed in 27 patients. The ethmoidal, maxillary, frontal and sphenoid sinuses were affected in 21, 18, three and two patients, respectively. Various degrees of nasal septum perforation were noted in 18 cases. In six of the 18 patients biopsied, the biopsy specimen showed involvement by lepromatous leprosy. **CONCLUSION:** These findings suggest that although these lepromatous leprosy patients had been treated, persistent infection was still commonly encountered. Paranasal sinus CT examination is a useful method for the evaluation of patient response to treatment and follow up; however, a CT scan alone cannot determine whether the leprosy is active.

Literatura corrente em hanseníase

Ranque B, Nguyen VT, Vu HT, Nguyen TH, Nguyen NB, Pham XK, Schurr E, Abel L, Alcais A. Age is an important risk factor for onset and sequelae of reversal reactions in Vietnamese patients with leprosy. *Clin Infect Dis* 2007; 44(1): 33-40.

BACKGROUND: Reversal, or type 1, leprosy reactions (T1Rs) are acute immune episodes that occur in skin and/or nerves and are the leading cause of neurological impairment in patients with leprosy. T1Rs occur mainly in patients with borderline or multibacillary leprosy, but little is known about additional risk factors. **METHODS:** We enrolled 337 Vietnamese patients with leprosy in our study, including 169 subjects who presented with T1Rs and 168 subjects with no history of T1Rs. A multivariate analysis was used to determine risk factors for T1R occurrence, time to T1R onset after leprosy diagnosis, and T1R sequelae after treatment. **RESULTS:** Prevalence of T1Rs was estimated to be 29.1%. Multivariate analysis identified 3 clinical features of leprosy associated with T1R occurrence. Borderline leprosy subtype e (odds ratio, 6.3 [95% confidence interval, 2.9-13.7] vs. polar subtypes) was the major risk factor; 2 other risk factors were positive bacillary index and presence of > 5 skin lesions. In addition, age at leprosy diagnosis was a strong independent risk factor for T1Rs (odds ratio, 2.4 [95% confidence interval, 1.3-4.4] for patients aged > or = 15 years old vs. < 15 years old). We observed that T1Rs with neuritis occurred significantly earlier than pure skin-related T1Rs. Sequelae were present in 45.1% of patients who experienced T1Rs after treatment. The presence of a motor or sensory deficit at T1R onset was an independent risk factor for sequelae, as was the age at diagnosis of leprosy (odds ratio, 4.4 [95% confidence interval, 1.7-11.6] for patients > or = 20 years old vs. < 20 years old). **CONCLUSION:** In addition to specific clinical features of leprosy, age is an important risk factor for both T1R occurrence and sequelae after treatment for T1Rs.

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Kharkar V, Bhor UH, Mahajan S, Khopkar U. Type I lepra reaction presenting as immune reconstitution inflammatory syndrome. *Indian J Dermatol Venereol Leprol* 2007; 73(4): 253-6.

Immune reconstitution inflammatory syndrome (IRIS) is an unusual inflammatory reaction due to infectious and non-infectious causes occurring in human Immunodeficiency virus (HIV)-infected patients. IRIS occurs after the initiation of antiretroviral therapy. There are no reports of type I lepra reaction due to IRIS in published literature from India. We report two cases of HIV-infected males who presented with borderline tuberculoid leprosy in type 1 reaction after the initiation of highly active antiretroviral treatment (HAART). Case 1 presented with multiple, tender, erythematous and hypoesthetic plaques on the trunk and extremities after 3 months of antiretroviral therapy. In case 2, type I lepra reaction was observed 2 months after the initiation of HAART.

Arora SK. Leprosy in a preschool child--a case report. *J Indian Med Assoc* 2007; 105(3): 140.

Leprosy in a preschool child appearing at the age of four years is reported due to its rarity, particularly at a time when we are hoping for its elimination. A 5-year-old female child presented with an erythematous rash over her right buttock for last one year. Histopathological examination from the patch revealed it to be a case of indeterminate leprosy. The child responded favourably with antileprosy treatment.

Said G. Infectious neuropathies. *Neurol Clin* 2007; 25(1): 115-37.

Peripheral neuropathies can result from several infective agents, ranging from viruses, especially retroviruses, to parasites and bacilli. Leprosy, which often is considered a disorder of the past, still is common in some geographic areas, especially in Africa, South America, and Asia. An increasing number of cases of neuropathies occurs in patients who have HIV or Lyme disease. The important point is that all these neuropathies are treatable and often preventable.

Pardillo FE, Fajardo TT, Abalos RM, Scollard D, Gelber RH. Methods for the classification of leprosy for treatment purposes. *Clin Infect Dis* 2007; 44(8): 1096-9.

The World Health Organization advocates 2 leprosy treatment regimens on the basis of disease classification (as multibacillary or paucibacillary) by skin lesion count. This method, which, in the Philippines, results in a high prevalence (78%) of patients with multibacillary leprosy, was directly compared with classification using standard histopathological and microbiological criteria in 264 currently untreated patients with leprosy. Of those whose leprosy was classified as paucibacillary, 38%-51% of patients had multibacillary leprosy according to classic criteria and were thus at risk of undertreatment according to World Health Organization recommendations.

Haroon N, Agarwal V, Aggarwal A, Kumari N, Krishnani N, Misra R. Arthritis as presenting manifestation of pure neuritic leprosy--a rheumatologist's dilemma. *Rheumatology* 2007; 46(4): 653-6.

Leprosy classically presents with cutaneous and neurological manifestations. In diagnosed cases of leprosy, rheumatological involvement varies from 1% to 70%. A primary articular presentation without cutaneous manifestations is not yet known. Herein, we present our experience of five cases of leprosy that presented with predominant articular involvement in the absence of cutaneous manifestations. **METHODS:** The study was conducted in the Department of Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences located in the state of Uttar Pradesh, one of the nine endemic states in India. Case records of patients with a definite diagnosis of leprosy were screened for the presenting manifestations, pattern of articular involvement, tenosynovitis, neurological signs and symptoms. Reports of nerve conduction study (NCS), nerve and synovial biopsy and other diagnostic tests were retrieved from laboratory records. Available radiographs were examined for evidence of juxta-articular osteopenia and erosions. **RESULTS:** Case records of 11,740 patients were screened, of which 28 had a diagnosis of leprosy. Twenty patients had presented with rheumatological complaints primarily. Five of the patients who presented with inflammatory arthritis with/without tenosynovitis (n = 4) and tenosynovitis alone (n = 1) had pure neuritic leprosy. All of these patients had thickened peripheral nerves and abnormal NCS. Sural nerve biopsy confirmed the diagnosis of leprosy in all these cases. **CONCLUSION:** A combination of tenosynovitis and thickened nerves in association with symmetric polyarthritis should raise a suspicion of leprosy even in the absence of cutaneous features.

Literatura corrente em hanseníase

Javaud N, Belenfant X, Stirnemann J, Laederich J, Ziol M, Callard P, Ronco P, Rondeau E, Fain O. Renal granulomatoses: a retrospective study of 40 cases and review of the literature. *Medicine (Baltimore)*; 86(3): 170-80.

Resumo: Renal granulomatoses represent 0.5%-0.9% of nephropathies examined by renal biopsies. Granulomas can be isolated to the kidney or associated with other tissue involvement. We describe 40 consecutive patients with renal granulomatoses, associated with pauci-immune crescentic glomerulonephritis in 2 patients and with vasculitis in another, seen in northeastern Paris hospitals between January 1991 and February 2004. The criterion for inclusion was the presence of 1 or more epithelioid granulomas in the renal interstitium. Our population of 25 men and 15 women had a median age of 53 years. All patients suffered from renal insufficiency with median creatininemia of 236.8 micromol/L (range, 124-805 micromol/L), associated with hypertension (25%), median proteinuria of 0.6 g/24 h (range, 0.08-3.00 g/24 h), microscopic hematuria (15%) and leukocyturia (22.5%). Histologic examination of extrarenal specimens detected granulomas in 82.4% of the bronchial biopsies taken, and in 100% of the 2 skin biopsies, the 2 lymph-node biopsies, and the liver and colon biopsies. The following etiologies were retained: sarcoidosis for 20 (50%) patients, drug-induced for 7 (17.5%), tuberculosis for 3 (7.5%), Wegener granulomatosis for 2 (5%), and leprosy, *Mycobacterium avium* infection, and Crohn disease for 1 (2.5%) patient each. No etiology could be identified for 5 (12.5%) patients. Treatment must be adapted to the etiology of each case. The renal outcome after treatment was generally favorable, with the estimated median creatinine clearance increasing from 26 mL/min (range, 5.4-80.0 mL/min) to 46.5 mL/min (range, 0-118 mL/min) after a median follow-up of 35.5 months (range, 3-158 mo). Nonetheless, 32 patients had persistent renal insufficiency; 1 required hemodialysis and another underwent renal transplantation. Sarcoidosis and medications are the most common causes of renal

granulomatosis. Idiopathic and drug-induced forms do not relapse after treatment discontinuation, and remission persists at long-term follow-up.

Annigeri SR, Metgud SC, Patil JR. Lepromatous leprosy of histoid type. *Indian J Med Microbiol* 2007; 25(1): 70-1.

Histoid leprosy is a variant of lepromatous leprosy, which develops as a result of resistance to dapsone monotherapy. Here we report two cases of lepromatous leprosy of histoid type, one with typical and another with atypical presentations.

Bretan O, Souza LB, Lastória JC. Laryngeal lesion in leprosy and the risk of aspiration. *Lepr Rev* 2007; 78(1): 80-1.

Leprosy affects the larynx, damaging its mucosa and sensory nerves and loss of sensation may result in aspiration of food and secretions. The laryngeal lesion may be insidious. Post-mortem studies showed bronchopneumonia that could have originated from aspiration. In patients with laryngeal symptoms, dysphagia or aspiration pneumonia loss of laryngeal sensation should be looked for.

Cuevas J, Rodríguez-Peralto JL, Carrillo R, Contreras F. Erythema nodosum leprosum: reactional leprosy. *Semin Cutan Med Surg* 2007; 26(2): 126-30.

The different clinical forms of leprosy are mainly related to the variety of immunological responses to the infection. Thus, lepromatous leprosy occurs in patients with a poor cell-mediated immunity to *Mycobacterium leprae*, whereas tuberculoid leprosy is associated with a high resistance to leprosy bacillus. Intermediate forms, including borderline tuberculoid leprosy, borderline lepromatous leprosy, and borderline leprosy, are a continuous and unstable spectrum of the disease. Leprosy reactions are rare and not well-known states that interrupt the usual chronic course and clinical stability of patients with leprosy. They are expressions of immunological perturbations. Attending to the clinical and histopathological manifestations, leprosy reactions may be separated in 2 or 3 different variants: revers e reaction (type I), erythema nodosum leprosum (type II), erythema polymorphous (type II) and Lucio's phenomenon, mainly considered a type II reaction, but sometimes designated type III. Type I leprosy reaction, also named [quot]upgrading reaction,[quot] occurs in borderline leprosy states and is associated with a shift toward the tuberculoid pole. Type II reaction usually occurs in lepromatous leprosy, and there are 3 different clinical variants, including erythema nodosum leprosum, erythema polymorphous-like reaction, and Lucio's phenomenon.

Flower C, Gaskin D, Marquez S. A case of recurrent rash and leg numbness mimicking systemic rheumatic disease: the occurrence of leprosy in a nonendemic area. *J Clin Rheumatol* 2007; 13(3): 143-5.

Leprosy, a rare chronic granulomatous communicable disease caused by *Mycobacterium leprae*, is classically known to have cutaneous and neurologic sequelae. As a result of immigration, the disease, endemic in Brazil, India, Nepal, Madagascar, Myanmar, and Indonesia, has been recognized to be present in North America and the Caribbean. We describe a case of a woman presenting with a long history of a recurrent rash and leg numbness, initially diagnosed with systemic lupus, who was later proven to have lepromatous leprosy. It is a reminder that this underappreciated disease should still be considered in the differential diagnosis of skin rash and neuropathy, even in nonendemic regions.

Thaipisuttikul Y, Kateruttanakul P. Sarcoidosis mimics lepromatous leprosy: a case report. *J Med Assoc Thai* 2007; 90(1): 171-4.

A 34-year-old Thai man presented with a two years history of progressively enlarged lepromatous leprosy like nodules and plaques on his back, chest, and scalp. Skin biopsy showed diffuse nonnecrotizing granulomatous inflammation with numerous multinucleated giant cells, lymphocytes, and plasma cells infiltration. The missed diagnosis of leprosy was made and was treated with antilepromatous drugs for one year. After repeated skin biopsy, the diagnosis was compatible with sarcoidosis. He was treated with prednisolone 40 mg per day for two weeks. The lesions gradually decreased in size and were controlled with prednisolone 10 mg per day.

Literatura corrente em hanseníase

Fenniche S, Benmously R, Sfia M, Daoud L, Debbiche A, Ben Ayed M, Mokhtar I. Vasculite cutanée a révélation tardive après guérison d'une lèpre lépromateuse diffuse: le phénomène de Lucio. *Med Trop* 2007; 67(1): 65-8.

O Lucio's phenomenon is an uncommon type 2 reactional state occurring exclusively in patients with diffuse lepromatous leprosy (Lucio-Latapi leprosy). Previous case reports have been most frequent in Central America and rare in Asia and Africa. Lucio's phenomenon is characterized by necrotic ulcerations of the skin preferentially on the lower extremities usually in association with ongoing Lucio lepromatosis. The purpose of this report is to describe an unusual case of Lucio's phenomenon occurring four years after successful treatment of diffuse lepromatous leprosy. The patient was a 51-year-old man who had presented diffuse lepromatous leprosy ongoing since 1998. Diagnosis was documented based on histological and bacteriologic evidence. After successful treatment using dapsone (100 mg/d), rifadine (600 mg/month) and ethionamide (250 mg/d), the patient was lost from follow-up for 4 years. In January 2005, he consulted again for alteration of general status. Clinical examination showed inflammatory livedo on the lower extremities in association with several infiltrating maculo-papular lesions and painful erythematous-purpuric lesions on the legs and buttocks. The patient's skin was dry, shiny and scaly with alopecia of the eyelashes and eyebrows. Examination of smear samples (skin and nasal) to identify mycobacterium leprae was negative. Histological study demonstrated epidermic necrosis with aspects of leucocytoclastic vasculitis. No Virchow cells were detected and Ziehl staining was negative. Search for circulating immune complexes and antiphospholipid antibodies was negative. Diagnosis of Lucio's phenomenon was made and the patient was treated using prednisone at a dose of 1 mg/kg/d in association with rifampicine (600 mg/month) and dapsone (100 mg/d). Outcome was favorable after one month of treatment. Lucio's phenomenon has rarely been observed in Tunisia. To our knowledge this is the third case reported from

Tunisia and only 13 cases have been reported in the world since 1983. In all cases including the two from Tunisia, Lucio's phenomenon occurred during the course of treatment of ongoing Lucio-Latapi lepromatous leprosy (2). The remarkable features of our case are that Lucio's phenomenon occurred a long time after successful treatment of lepromatous leprosy and that the patient responded promptly to treatment. The pathogenesis of Lucio's phenomenon is often compared with that of erythema nodosum leprosum. Discussion focuses on pathophysiologic features and natural course of Lucio's phenomenon.

Coeytaux A, Truffert A, Mueller Y, Antille C, Jackson Y. La lèpre, une maladie neurologique. *Rev Med Suisse* 2007; 3(110): 1178.

Leprosy is a treatable chronic infectious disease, caused by *Mycobacterium leprae*, not highly transmissible that affects mainly the skin and peripheral nerves. Often neglected because it is rare in western countries, it may be encountered in patients coming back from endemic areas. Diagnostic criteria include underpigmented patches with loss of sensation, thickened peripheral nerves and acid-fast bacilli on skin smears or biopsy material. The variation of the cellular immune response determines the different forms of the disease (tuberculoid to lepromatous) and the neurological impairment. A precise diagnosis is mandatory to adjust the treatment. Among the neurological complications the leprosy reactions are the most important because they may result in increased nerve damage and compromised recovery if the specific treatment is delayed.

CONTROLE

Oskam L, Mi B. Report of the workshop on the use of chemoprophylaxis in the control of leprosy held in Amsterdam, The Netherlands on 14 December 2006. *Lepr Rev* 2007; 78(2): 173-85.

In recent years a number of field trials have been carried out to assess the efficacy of rifampicin chemoprophylaxis for the prevention of leprosy in contacts of leprosy patients. Results from these trials are now being analysed and published. The aim of this one-day workshop was to review current evidence and discuss potential future courses of action with regard to the use of chemoprophylaxis to prevent leprosy. During the morning session the current evidence for the contribution that chemoprophylaxis may make to leprosy prevention was presented, both the results from trials (abstracts in section 1) and the outcome of modelling (abstract in section 2); in addition presentations were given on different aspects of the use of antibiotics for chemoprophylaxis (abstracts in section 3). The afternoon was devoted to discussions, a summary of which is presented in section 4 of this report. The conclusions and recommendations are given in section 5.

Nery JA, Lehman LF, Schreuder PA. Role of dermatologists in leprosy elimination and post-elimination era. *Lepr Rev* 2007; 78(1): 41-2.

Would it not have been better to have left out the word 'elimination' altogether in the question and do what WHO has done in its new strategic plan for 2006-2010, 'Global Strategy for further reducing the Leprosy Burden and Sustaining Leprosy Control Activities'? Why not use a title such as 'The Role of Dermatologists in reducing the Leprosy Burden and Sustaining Leprosy Control Activities'? Some elements of the 'foundation' of the elimination policy have been (and are still) very controversial, its definition and the unsubstantiated (up till now) claim that when reaching a prevalence rate of less than 1 per 10,000, the transmission of the infection would be interrupted and the incidence would therefore decline.

Faye O, Hay RJ, Ryan TJ, Keita S, Traore AK, Mahe A. A public health approach for leprosy detection based on a very short term-training of primary health care workers in basic dermatology. *Lepr Rev* 2007; 78(1): 11-6.

INTRODUCTION: In countries where leprosy control is integrated to general health services, health workers, at primary health care level, often manage a large number of patients with skin diseases including leprosy. The distinction of leprosy from other skin diseases requires more skill and attention. Basic dermatological knowledge will help these staff to provide a better quality of care. A few years ago, a short term training programme focussed on leprosy and some common skin diseases was set up in Mali through a pilot project. This study will evaluate the impact of this training on the detection of leprosy at primary health care level. **METHODS:** health care workers from two health districts were invited to participate in the training. Trainee was submitted to an anonymous written test before training, immediately after and 12-18 months post-training using a standardized scoring system. The suspected or referred leprosy cases before and after training were compared. Data were recorded and analysed with the software Epi info version 6.04. **RESULTS:** Overall, 495 HCW attended the three anonymous written tests (before training, just after and 12-18 months later). The proportion of participants who gave correct answers before training, just after were respectively: 33 and 57% for correct diagnosis, 5 and 39% for test of sensation and 28 and 47% for referral. Eight patients suspected of leprosy were referred for further examination; in these, five cases of leprosy were detected. **DISCUSSION:** The training showed a huge improvement in the skill of the participants in managing leprosy patients. This study addresses how leprosy control can be improved by involving primary health care staff and by the implementation of only a single day's training on basic dermatology. **CONCLUSION:** The role of the dermatologist in this post-elimination era of leprosy needs to be reconsidered and adapted to the increasing need to take multiple programmes, inclusive of dermatology and leprosy, into primary health care services and those interested in leprosy control should fund these programmes.

Literatura corrente em hanseníase

Oliveira ML, Penna GO, Telhari S. Role of dermatologists in leprosy elimination and post-elimination era: the Brazilian contribution. *Lepr Rev* 2007; 78(1): 17-21.

Dermatologists in Brazil have always been involved in care of leprosy patients, and have been alternating with public health physicians in the management of control policies. It is worth mentioning that Fernando Terra, founder of the Brazilian Society of Dermatology (BSD) in 1912, established the position of intern dermatologist at the Hospital dos Lizardos, in Rio de Janeiro, in 1913 (Souza-Araújo, 1952; Oliveira, 1991). In 1920, the dermatologist Eduardo Rabello formulated the first national public policy on the control of leprosy in the country, which was called 'Inspection of Prophylaxis of Leprosy and Venereal Diseases'. His son was an enthusiast of dermatological research and his main legacy was the polarity concept of leprosy (Rabelo, 1937). However, from 1930 to 1985, the public health physicians were in charge of the political guidelines that represented the period of establishing the vertical programmatic structure, with compulsory isolation of patients (1933-1962). Moreover, the federal states coordinated the control actions, based on the leprosy prophylaxis campaign. The dermatologists resumed the conduction of the control process in 1986, when multi-drug therapy (MDT) was implemented in the country, and in 1991, when decentralization of public healthcare services to the municipal level took place. In 2003 again, the dermatologists were no longer in control of the national policy. However, active dermatologists have acted in Brazilian references on diagnosis and treatment of Hansen's disease, at municipal, state and national levels. It is true that dermatologists have been getting away from leprosy control actions. And one could ask: who will replace this specialist? In the 'post-elimination' era, when the public primary healthcare technicians no longer consider leprosy of much significance, the knowledge of the expert in this disease and its differential diagnoses will be crucial.

Kawuma HJ. Potential role of dermatologists and dermatological services in developing and sustaining the leprosy control referral system in resource constrained settings. *Lepr Rev* 2007; 78(1):34-7.

General Health Services that pay due attention to the management of skin conditions are opportune for suspecting and diagnosing early leprosy. In many developing countries, patients with dermatological conditions can only access specialist services in the larger cities and university hospitals; unaffordable costs make the services even less accessible if they can only be provided in the private sector. The high profile of dermatologists in the health services, gives them the opportunity to facilitate the development and implementation of a referral system that includes leprosy. This potential benefit for leprosy control must be initiated by current National Leprosy Programme Managers through establishing formal relationships with the dermatologists and involving them and other partners in the re-designing of leprosy control strategies to keep them in tandem with changing epidemiological patterns, national policies and on-going health sector reforms. The same health service managers should avail of the opportunities from the dermatologists (both in public and private sectors) about the current knowledge on the management and control of leprosy.

[Mh] Termos MeSH: Controle de Doenças Transmissíveis/EC/*MT/TD

Ignotti E, Bayona M, Alvarez-Garriga C, Andrade VL, Valente JG. Transmission of Hansen's disease and unscreened household contacts. *Indian J Lepr* 2007; 79(1): 11-25.

INTRODUCTION: Leprosy household contact investigation has been recommended as an epidemiological surveillance strategy for more than 50 years. **OBJECTIVE:** The purpose of this study was to estimate the yield that could be achieved in case detection if four contacts could be examined for every case found. **METHODS:** For the estimation of the number of cases not detected (lost) and yield per contact investigation in Mato Grosso, the incidence rates and yield calculations from a cohort study conducted in Rio de Janeiro by Matos et al (1999) were applied to data from the state of Mato Grosso. Also, to identify high-risk groups for leprosy, a cross-sectional study was conducted in which leprosy cases found as a result of a contact investigation were compared with index cases detected by other means. **RESULTS:** The lost cases among household contacts were at least 4 per every 10 new cases detected. This is the result of insufficient contact investigations - it being 0.8 instead of 4 contact investigations per each case as recommended by the Brazilian Ministry of Health. Up to 60% of the incidence of leprosy could be explained by the high number of lost cases among household contacts not examined. Women and children are more likely to be contacts. **CONCLUSION:** The lost cases due to insufficient contact investigation represent lost opportunities in early detection and treatment, thus losing the opportunity to reduce leprosy transmission.

Bührer-Sékula S, Visschedijk J, Grossi MA, Dhakal KP, Namadi AU, Klatser PR, Oskam L. The ML flow test as a point of care test for leprosy control programmes: potential effects on classification of leprosy patients. *Lepr Rev* 2007; 78(1): 70-9.

OBJECTIVE: To evaluate the use of the ML Flow test as an additional, serological, tool for the classification of new leprosy patients. **DESIGN:** In Brazil, Nepal and Nigeria, 2632 leprosy patients were classified by three **METHODS:** (1) as multibacillary (MB) or paucibacillary (PB) according to the number of skin lesions (WHO classification), (2) by slit skin smear examination, and (3) by serology using the ML Flow test detecting IgM antibodies to *Mycobacterium leprae*-specific phenolic glycolipid-I. **RESULTS:** The proportion of MB leprosy patients was 39.5, 35.6 and 19.4% in Brazil, Nepal and Nigeria, respectively. The highest seropositivity in patients was observed in Nigeria (62.9%), followed by Brazil (50.8%) and Nepal (35.6%). ML Flow test results and smears were negative in 69.1 and 82.7% of PB patients, while smears were positive in 58.6% of MB patients in Brazil and 28.3% in Nepal. In MB patients, both smears and ML Flow tests were negative in 15.6% in Brazil and 38.3%, in Nepal. Testing all PB patients with the ML Flow test to prevent under-treatment would increase the MB group by 18, 11 and 46.2% for Brazil, Nepal and Nigeria, respectively. Using the ML Flow test as the sole criterion for classification would result in an increase of 11.3 and 43.5% of patients requiring treatment for MB leprosy in Brazil and Nigeria, respectively, and a decrease of 3.7% for Nepal. **CONCLUSIONS:** The ML Flow test could be used to strengthen classification, reduce the risk of under-treatment and minimize the need for slit skin smears.

Literatura corrente em hanseníase

Rao PV, Rao SL, Vijayakrishnan B, Chaudhary AB, Peril S, Reddy BP, Reddy GS. Knowledge, attitude and practices about leprosy among medical officers of Hyderabad urban district of Andhra Pradesh. *Indian J Lepr* 2007; 79(1): 27-43.

In India, MDT was implemented through vertical programme staff of the National Leprosy Eradication Programme till the year 2001, when it was integrated into general health services (GHS). Human resource development of GHS is a vital, preparatory action for successful integration of leprosy into GHS. District Technical Support Teams (DTST) have been formed with responsibility for building the capacity of medical and paramedical staff of urban health posts (UHPs). In this context, it is necessary to know the current levels of Knowledge, Attitude and Practices (KAP) about leprosy prevailing among health staff at a given point in time, so that required knowledge and skills can be imparted, if need be. The present study is an attempt in this direction for assessing the KAP status of health staff working in Hyderabad city. 402 staff members (352 females and 50 males) working in urban health posts, the Employees State Insurance Corporation and the Central Government Health Services dispensaries in Hyderabad urban district in Andhra Pradesh were included in the study carried out in 2004 in order to assess KAP, and some operational parameters. A questionnaire was used to elicit responses of 110 medical officers in urban Hyderabad and the data were analysed and discussed. Medical officers have shown consistent higher knowledge on leprosy, followed by nursing staff as compared to other paramedical workers. Only 40% of the medical officers had the opportunity of seeing at least 1 case of leprosy in their practice. Medical Officers who received training in leprosy and possessed reference material on leprosy have shown higher knowledge and practice. More than half of the study subjects did not have specific training in leprosy. Two major operational problems expressed by the medical officers were managing big crowds in OPD and time lost in meetings. 96 (87.3%) of 110 medical officers felt integration of leprosy services into general health services can be

effectively implemented. 78 (71%) expressed that a leprosy patient with severe reaction needed priority attention at the out-patient department indicating good understanding of reactions in leprosy and a positive attitude towards such patients. There is a need to organize training at regular intervals to cover new persons as well as reinforcing and updating the knowledge of those already trained.

Canicoba M, Feldman N, Lipovetzky S, Moyano O. Evaluación del estado nutricional de pacientes en un hospital con lepra en Argentina. *Nutr Hosp* 2007; 22(3): 377-81.

INTRODUCTION: Leprosy is a regional problem of public health in the Argentine Republic. It has seen a continuous decrease of the prevalence in the last 10 years, with value is about 0.17/10000 citizen and the detection rate is constant about 0.10/10000 citizen. Even the death rate is low, its importance is given for the physicals, socials, permanent and the progressive disabilities that its produce if there no early diagnostic and a regular and complete treatment. The Dr. Baldomero Sommer National Hospital, that give a complete assistance to the leprosy patients either to the pavilion patients or the ill patients that help themselves and live in houses with their families and where it is given food assistance to promote and increase their quality of life. **OBJECTIVES:** Evaluate The nutritional state of the ill patients that help themselves and live in houses with their families. Analyze the caloric and proteic brought by the institution. **MATERIAL AND METHODS:** It is a transversal and descriptive study. We made a nutritional evaluation of the patients that live in each of the 4 suburb of the hospital, whom has been previously appointed by the coordinator of the zone, with the porpoise of identify the nutritional state of each one of the patients, quantify the nutritional risk, and indicate, adequate and monitories the nutritional support. The diagnostic was realized by the dietician through: anthropometric parameters (weight, height and body mass index), biochemical parameters, according to the clinical history: albumin, cholesterol, urea, hematocrito and associated illness. **RESULTS:** We evaluated 219 patients of 246, with a middle age of 56.4 years, 62.2% males and 57.8% females. We detected that obesity was the nutritional disorder with mayor prevalence in these population (74.3%) and with mayor incidence in the moderate obesity in males and mayor incidence in severe obesity in females. The prevalence of malnourishment was 3.6% and well-nourished was 23.7%, 27 of the patients (10.9%) did not go to the nutritional evaluation. The

2.8% of the patients did not have an actual laboratory for more than 2 years. In the clinical histories, we found that the dosage of albumin in an average of 4.2 g/dl, and the 2.8% of the patients did not have any value of albumin. The values of hematocrito and urea determinate an adequate brought of proteins in the evaluated population. Inside the nutritional diagnostic we considerate the search of diabetes (present ion the 9.7% of the patients), dislipemia (present ion the 32.8% of the patients, taken a level of 200 mg / dl of cholesterol), chronic renal deficiency (present in the 9.3% of the patients), and arterial hypertension (present in the 33.6% of the patients). **CONCLUSIONS:** Exist a high prevalence of moderate-severe obesity in the studied population that have no coincidence with the universal literature. These data shows the necessity to adequate the caloric and proteic brought to the patients. The majority of the patients presented Dislipemia and or diabetes and or arterial hypertension. Promote the development of educational programs to better the nutritional state of the risk population, better the quality of life and reduce cardiovascular risks, using an international model that include strategies for the following of a health diet and an increase of physical activity.

DIAGNÓSTICO

Goulart IM, Cardoso AM, Santos MS, Gonçalves MA, Pereira JE, Goulart LR. Detection of Mycobacterium leprae DNA in skin lesions of leprosy patients by PCR may be affected by amplicon size. Arch Dermatol Res 2007; 299(5-6): 267-71.

Despite the high sensitivity and specificity of PCR for infectious disease diagnostics, it has presented low sensitivity for Mycobacterium leprae DNA detection in the tuberculoid pole (TT and BT) of leprosy. In order to demonstrate the effect of amplicon size on the efficacy of PCR detection of M. leprae DNA in skin lesions of leprosy patients, two pairs of primers targeting the M. leprae genomic DNA, RLEP3 (X17153), were used to amplify fragments of 372 and 130-bp until their PCR end-points were reached after 40 reaction cycles. Skin biopsies of leprosy lesions in 110 non-treated patients were used for bacilloscopy index (BI) analysis and PCR tests. The 130-bp fragment was detected in 73.6% of samples (81/110), and classified as TT (40%), BT (55.5%), and 100% of BB, BL and LL. The 372-bp fragment was detected in 52.7% and classified as TT (13.3%), BT (33.3%), BB (64.7%), BL (83.3%), and LL (95.2%). The BI of biopsies was positive in 39.1% of samples, classified as TT (0%), BT (2.2%), BB (64.7%), BL (91.6%), and LL (95.2%). The shorter amplicon (130-bp) has improved diagnosis by 20.9 and 34.5% in relation to the 372-bp fragment and the BI, respectively, and has shown a superior sensitivity (73.6%), specificity (100%) and accuracy (86.2%). The 130-bp amplicon could not detect % of positive BI of biopsies in BT cases. Therefore, for confirmatory diagnosis, we propose the use of PCR detection of the 130-bp genomic target, especially when the tuberculoid pole forms are considered, which has reached 51.6% of positivity in this group.

Nigam PK, Kumar P, Pathak N, Mittal S. Fine needle aspiration cytology in reactional and non-reactional leprosy. Indian J Dermatol Venereol Leprol 2007; 73(4): 247-9.

BACKGROUND: Histopathological evaluation of skin lesions is not feasible in many leprosy endemic areas. Fine needle aspiration cytology (FNAC) is a simpler tool compared to histopathology for the evaluation of the cytomorphology of skin lesions. AIMS: To study the cytomorphology of leprosy lesions in fine needle aspirates and correlate it with the histopathology. METHODS: Seventy leprosy patients diagnosed and classified according to Ridley Jopling scale were included. Fine needle aspirates were taken from the lesion followed by a skin biopsy from the same site for histopathological examination after H/E staining. RESULTS: Borderline leprosy patients with Type I reaction showed significantly large numbers of giant cells, collagen and elastin in their smears as compared to those without reaction. The smears were more heavily cellular with fragmented collagen and elastin along with significant increase in neutrophils in patients with Type II reaction while foamy macrophages with fatty background were common in non-reactional lepromatous leprosy patients. A complete correlation between histopathological and cytomorphological findings was observed in 77.3% of cases. CONCLUSION: FNAC may be used as an alternative tool to assess leprosy lesions in areas where histopathological services are not readily available.

Hari S, Subramanian S, Sharma R. Magnetic resonance imaging of ulnar nerve abscess in leprosy: a case report. *Lepr Rev* 2007; 78(2): 155-9.

A 14-year-old girl on multidrug treatment for borderline tuberculoid leprosy presented with a swelling in her left arm and soon thereafter developed ulnar claw hand. MRI showed a well-defined ovoid lesion arising from the left ulnar nerve, isointense to muscle on T1W images and hyperintense on T2W and STIR images. On post gadolinium T1W sequence the lesion showed peripheral rim enhancement with central necrosis suggestive of abscess. The ulnar nerve proximal and distal to the lesion was thickened and showed mild contrast enhancement. On aspiration the swelling yielded frank pus which was positive for acid-fast bacilli.

Dayal R, Agarwal M, Natrajan M, Katoch VM, Katoch K, Singh K, Chauhan DS. PCR and in-situ hybridization for diagnosis of leprosy. *Indian J Pediatr* 2007; 74(7): 645-8.

OBJECTIVE: To assess the diagnostic value of Polymerase Chain Reaction (PCR) and in situ hybridization. **METHODS:** This prospective study was carried out in 22 patients. **RESULTS:** The histopathological examination confirmed the clinical diagnosis in 27.2% cases only. In situ hybridization showed a positivity of 42.8% in early (I/BT) and 46.7% in BB/BL group. In situ hybridization thus enhanced the diagnosis by 18.1%. PCR targeting 36 kDa gene of *M. leprae* was performed on 15 cases. In these 15 cases, histopathology confirmed the diagnosis in 4 cases (26.6%) and PCR confirmed the diagnosis in 10 cases (66.6%), thus enhancing the diagnosis by 40%. **CONCLUSION:** 36 kDa PCR and in situ hybridization enhance the diagnosis of leprosy when compared to routine histopathology. They are important diagnostic tools for definitive diagnosis in early and doubtful cases of leprosy.

Villarroel MF, Orsini MB, Grossi MA, Antunes CM. Impaired warm and cold perception thresholds in leprosy skin lesions. *Lepr Rev* 2007; 78(2):110-21

The aim of the present study was to determine the frequency of alteration in warm perception thresholds (WPT), cold perception thresholds (CPT) and the warm and cold perception interval (WCPI) in leprosy-suspected skin lesions, and to determine if these tests could assist in the diagnosis of leprosy. Tests were conducted using a thermal sensory analyser TSA-2001 (Medoc Ltd, Israel) and the method of levels. A cross-sectional study of 112 patients presenting leprosy-suspected skin lesions ('patch'), with no clinical evidence of peripheral nerve damage, was conducted. Leprosy diagnosis was based on clinical dermatoneurological examinations and complementary tests. One hundred and eight subjects (45 males, 63 females; average age 37.7 years) completed the tests: 82 were positively diagnosed with leprosy and 26 with diseases of different etiologies. The mean values of WPT (45-63 +/- 5.59), CPT (9.64 +/- 11.34) and WCPI 36.01 +/- 15.58) registered in leprosy-skin lesions were significantly different ($P < 0.001$) from lesions of diverse aetiologies and skin area without lesions. The cut-off point for WPT as determined from the ROC curve (receiver operating characteristic) was 35-10 degrees C, with a sensitivity of 90.2% and a specificity of 100%, and the corresponding cut-off point for CPT was 28.95 degrees C, with a sensitivity of 92.7% and a specificity of 100%. Nevertheless, all patients with leprosy presented a WCPI greater than 6.10 degrees C (ROC curve) in skin lesions. Increase in the thermal thresholds indicated warm hypoaesthesia, cold hypoaesthesia or both. The WCPI, which embraces both warm and cold perception thresholds, was the best indicator of thermal sensation, a term used in literature as a non-specific expression that does not describe warm and cold stimuli explicitly in terms of units of temperature.

Literatura corrente em hanseníase

Villarroel MF, Orsini MB, Lima RC, Antunes CM. Comparative study of the cutaneous sensation of leprosy-suspected lesions using Semmes-Weinstein monofilaments and quantitative thermal testing. *Lepr Rev* 2007; 78(2): 102-9.

The objective of the present study was to compare the warm cold perception thresholds (WPT), cold perception thresholds (CPT) and the warm and cold perception interval (WCPI) determined in our previous study with the touch-pressure thresholds, in leprosy-suspected skin lesions ('patch'). Thermal testing was conducted using a thermal sensory analyser TSA-2001 (Medoc Ltd., Israel) and the method of levels. The touch-pressure thresholds were measured using Semmes-Weinstein monofilament (SWM) of 0.05g, 0.2g, 2g, 4g, 10g and 300g. A cross-sectional study of 112 patients presenting with leprosy-suspected skin lesions, with no clinical evidence of peripheral nerve damage, was conducted. Leprosy diagnoses were based on clinical dermatoneurological examinations. One-hundred-and-eight subjects (45 males, 63 females; average age 37.7 years) completed the tests: 82 were positively diagnosed with leprosy and 26 with diseases of different aetiologies. The SWM test showed a sensitivity of 81.7% and a specificity of 96.1%, while the warm and cold perception thresholds presented sensitivity of 90.2% and 92.2%, respectively (both with 100% specificity). In leprosy patients, lesions that exhibited pressure thresholds of 0.05g typically showed significantly different WPT, CPT and WCPI values when compared with skin lesions of different aetiologies. Within the leprosy group, the mean values of WPT, CPT and WCPI increased according to the increase in touch-pressure thresholds. Some of the patients exhibiting leprosy lesions with touch-pressure thresholds of 0.05 and 0.2g presented normal WPT or CPT values. However, all patients with SWM equal or above 2.0g presented altered WPT and CPT. All patients with leprosy, including those that exhibited pressure thresholds of 0.05g, presented altered WCPI in the skin lesions. Despite a higher sensitivity to thermal tests, the SWM has adequate validity as a screening tool in the diagnosis of cutaneous forms of leprosy

and in the selection of patients who should be submitted to a more detailed examination.

Bravo FG, Gotuzzo E. Cutaneous tuberculosis. *Clin Dermatol* 2007; 25(2): 173-80.

Cutaneous tuberculosis continues to be one of the most elusive and more difficult diagnoses to make for dermatologists practicing in developing countries. Not only because they have to consider a wider differential diagnosis (leishmaniasis, leprosy, actinomycosis, deep fungal infections, etc) but also because of the difficulty in obtaining a microbiological confirmation. Despite all the advances in microbiology, including sophisticated techniques such as polymerase chain reaction, the sensitivity of new methods are no better than the gold standard, that is, the isolation of *Mycobacterium tuberculosis* in culture. Even now, in the 21st century, we rely on methods as old as the intradermal reaction purified protein derivative (PPD) standard test and therapeutic trials, as diagnostic tools. In this situation, it is important to recognize the many clinical faces of cutaneous tuberculosis to prevent missed or delayed diagnoses.

Siddaraju N, Yaranal PJ. Use of fine needle aspiration cytology in leprotic lesions: a report of 4 cases. *Acta Cytol* 2007; 51(2): 235-8.

BACKGROUND: Although a few studies have shown fine needle aspiration cytology (FNAC) to be a sensitive diagnostic tool in the detection of nerve involvement, its role as an initial diagnostic procedure in pure neuritic leprosy (PNL) and in the detection of skeletal lesions with unusual findings has not been documented before. **CASES:** Three patients who presented with thickened nerves and a fourth with biopsy-proven lepromatous leprosy with lesions in hand bones underwent FNAC. Of the 3 patients with nerve thickening, 2 had a clinical suspicion or diagnosis of neuritic leprosy, whereas in the third patient a clinical differential diagnosis of a soft tissue tumor or parasitic cyst was considered. FNAC in all 3 cases revealed epithelioid cell granulomas, Langhans giant cells and caseous necrosis. Fites and Ziehl-Neelsen stains were negative for acid-fast bacilli. Cytologic diagnosis of pure neuritic leprosy was made in all 3 cases and confirmed by histopathologic examination. FNAC of skeletal lesions from the fourth patient confirmed involvement of bone with unusual cytologic findings of epithelioid cell granulomas and giant cells along with a significant proportion of foamy macrophages and strong Fites stain positivity. **CONCLUSION:** FNAC is a simple, useful, minimally traumatic and routinely applicable procedure in the diagnosis of pure neuritic leprosy and leprosy osteitis.

EPIDEMIOLOGIA

Autor: Ishii N, Nagaoka Y, Mori S, Suzuki K. Present leprosy situation in the world in 2006. *Nihon Hansenbyo Gakkai Zasshi* 2007; 76(1): 19-28.

The epidemiological situation of leprosy is reported by the health division of each country to WHO. The reported data is collected by WHO and is immediately run on the Weekly Epidemiological Record. On this latest edition, data from the beginning of 2006 was reported. Early case detection and treatment with multidrug therapy (MDT) remains the cornerstone of leprosy control. The challenge will be to establish these facilities as part of an integrated system that provides referral services for other diseases in the area.

Kumar A, Girdhar A, Girdhar BK. Incidence of leprosy in Agra district. *Lepr Rev* 2007; 78(2):131-6.

This study presents estimates of incidence of leprosy among the familial contacts (FC) and non-familial contacts (NFC) of leprosy patients in Agra, a district endemic for leprosy. The study covers 42,113 persons followed up for 123,951.2 person years (PY) during which 77 individuals developed leprosy giving an incidence of 6.2/10,000 PY in the total leprosy-free population studied (TLPS). The incidence rate in NFCs was observed to be 4.6/10,000 PY while the FCs had a significantly higher incidence rate of 67.6/10,000 PY ($P < 0.001$). Incidence rate among the FC of paucibacillary leprosy (PB) patients was 41.0/10,000 PY while the corresponding figure for multibacillary leprosy (MB) contacts was 131.3/10,000 PY ($P < 0.05$). Applying methods of survival analysis, the incidence rate at the end of 1 year was observed to be 4-0 (per 10,000), increased to 12.0 by 2 years and 18.0 at the end of 3 years in TLPS. The incidence rate was almost similar in both the sexes and was found to increase significantly with age. The observations clearly indicate that leprosy is still endemic in the area and transmission continues.

Literatura corrente em hanseníase

Penna ML, Penna GO. Trend of case detection and leprosy elimination in Brazil. *Trop Med Int Health* 2007; 12(5): 647-50.

Only six countries did not meet the leprosy elimination target during 2005, amongst them Brazil. In 2006, the Brazilian Ministry of Health announced a reduction of the detection rate of 24% or 10 900 cases from 2004 to 2005. A negative binomial parabolic regression model was adjusted to the detection rate historical series from 1980 to 2004, in order to predict the 2005 detection rate and its 95% confidence interval. This analysis showed that the number of new leprosy cases for 2005 could not be predicted from the previous behaviour of the data what calls for an epidemiological or operational explanation hypothesis. The hypothesis that this drop in detected case number is due to operational change, as a reduction in diagnosis or a modification in the reporting routine, is more likely. Recent change in prevalence case definition turned the prevalence ratio a function of only one variable, the detection rate, as the duration of the diagnosed disease became fixed. In the early nineties, based on epidemiological data evaluation, the BMoH recognized the impossibility of reaching the elimination goal, but it committed to seek leprosy control. This position changed after some years. Leprosy Elimination is a strategy supported by the national and international public opinion. As a one for all recipe, it may cause unwanted effects for it is not flexible enough to deal with different epidemiological behaviours and public health traditions.

Owen R, Roche PW, Hope K, Yohannes K, Roberts A, Liu C, Stirzaker S, Kong F, Bartlett M, Donovan B, East I, Fitzsimmons G, McDonald A, McIntyre PB, Menzies RI. Australia's notifiable diseases status, 2005: annual report of the National Notifiable Diseases Surveillance System.

In 2005, 60 diseases and conditions were nationally notifiable in Australia. States and territories reported a total of 125,461 cases of communicable diseases to the National Notifiable Diseases Surveillance System: an increase of 10% on the number of notifications in 2004. In 2005, the most frequently notified diseases were sexually transmissible infections (51,557 notifications, 41% of total notifications), gastrointestinal diseases (29,422 notifications, 23%) and bloodborne diseases (19,278 notifications, 15%). There were 17,753 notifications of vaccine preventable diseases; 4,935 notifications of vectorborne diseases; 1,826 notification of other bacterial infections (legionellosis, leprosy, meningococcal infections and tuberculosis) and 687 notifications of zoonotic diseases.

Distribuição por Sexo

Desikan KV, Sudhakar KS, Tulasidas I, Rao PV. Observations on reactions of leprosy in the field. *Indian J Lepr* 2007; 79(1): 3-9.

In order to assess the incidence of reaction in leprosy, it would be necessary to examine the data from a field control unit. In this study, it was found, at a fully monitored control unit, that Type I reaction occurred in 3.9% of borderline cases and Type II in 23.7% of LL and BL cases. Even so, the load of reaction is not high since reaction of Type I and Type II together are seen only in 3.7% of all types of cases. A majority of them are of mild or moderate degree and could be treated as out-patients. Of the borderline cases, the BB type showed maximum rate of reaction. The BL type can present with both Type I and Type II reactions with a total incidence of 12.8%. While the BT type constituted 74% of total cases, reaction of Type I occurred in 3.1% of cases. Reaction also occurred in 0.8% of RFT cases.

Chen S, Zheng Y, Zheng M, Wang D. Rapid survey on case detection of leprosy in a low endemic situation, Zhucheng County, Shandong Province, The People's Republic of China. *Lepr Rev* 2007; 78(1): 65-9.

The prevalence of leprosy fell below 1 per 100,000 in Shandong province in 1994. Since then, a few incident leprosy cases have been reported each year over the past 10 years. In order to explore whether or not the reduction in case detection in the province was due to the stopping of active case-finding activities, a rapid village survey was conducted in a formerly endemic county, using skin disease service. Ninety-one villages in 23 townships, covering a total population of 104,885, were surveyed. No leprosy case was detected. The results of the survey, along with other evidences, such as higher MB/PB ratio among newly detected cases and late onset of the disease, suggest that leprosy is dying out as a disease in the county as well as in Shandong. The efforts of the leprosy control programme should shift to other services such as prevention of disability and care for the disabled.

Nobre V, Guedes AC, Proietti FA, Martins ML, Nassif G, Serufo JC, Lambertucci JR. Increased prevalence of human T cell lymphotropic virus type 1 in patients attending a Brazilian dermatology clinic. *Intervirology* 2007; 50(4): 316-8.

Brazil may have the highest absolute number of individuals infected by human T cell lymphotropic virus type 1 (HTLV-1). It has been suggested that the prevalence of HTLV-1 is increased in patients with skin diseases. This study shows a higher prevalence of this infection in 1,229 patients attending a Brazilian dermatology clinic (0.7%) when compared to blood donors (0.22%). Of note, one additional patient tested positive for HTLV-2. The main skin diseases described in HTLV-1 seropositives were vitiligo (2 cases), dermatophytosis (2 cases), and leprosy (2 cases). A 23-year-old woman received a diagnosis of infectious dermatitis.

GENÉTICA

Martiniuk F, Tambini M, Rahimian J, Moreira A, Yee H, Tchou-Wong KM, Hanna BA, Rom WN, Levis WR. Identification of novel hsp65 RFLPs for *Mycobacterium leprae*. *J Drugs Dermatol* 2007; 6(3): 268-74.

Leprosy or Hansen's disease is a chronic infectious disease caused by an acid-fast bacillus, *Mycobacterium leprae* (*M. leprae*). The bacilli proliferate in macrophages infiltrating the skin and gain entry to the dermal nerves via the laminar surface of Schwann cells where they replicate. After entry, the Schwann cells proliferate and then die. Conclusive identification of *M. leprae* DNA in a sample can be obtained by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) for the heat shock 65 gene (*hsp65*). Molecular epidemiology will make it possible to study the global distributions of *M. leprae*, explore the relationship between genotypes-incidence rates, mode of transmission, and the type of disease (tuberculoid vs. lepromatous). We amplified DNA using PCR for the *hsp65* gene from 24 skin lesions from patients diagnosed with various types of leprosy. Fifteen out of 24 were positive for the *hsp65* gene. Digestion with *HaeIII*-PAGE for the RFLP confirmation of the presence of *M. leprae* DNA showed the typical pattern in 5 out of 24 and 2 novel patterns in 10 out of 24 patients. We confirmed the presence of *M. leprae* DNA by sequencing the genes for *gyraseA* or *B* and *folP*, which contained only *M. leprae* specific single nucleotide polymorphisms (SNPs). Thus, we describe novel *hsp65* RFLPs for *M. leprae* found in a high frequency making them ideal for future epidemiology and transmission studies.

Literatura corrente em hanseníase

Alcais A, Alter A, Antoni G, Orlova M, Nguyen VT, Singh M, Vanderborght PR, Katoch K, Mira MT, Vu HT, Ngyuen TH, Nguyen NB, Moraes M, Mehra N, Schurr E, Abel L. Stepwise replication identifies a low-producing lymphotoxin-alpha allele as a major risk factor for early-onset leprosy. *Nat Genet* 2007; 39(4): 517-22.

Host genetics has an important role in leprosy, and variants in the shared promoter region of PARK2 and PACRG were the first major susceptibility factors identified by positional cloning. Here we report the linkage disequilibrium mapping of the second linkage peak of our previous genome-wide scan, located close to the HLA complex. In both a Vietnamese familial sample and an Indian case-control sample, the low-producing lymphotoxin-alpha (LTA)+80 A allele was significantly associated with an increase in leprosy risk ($P = 0.007$ and $P = 0.01$, respectively). Analysis of an additional case-control sample from Brazil and an additional familial sample from Vietnam showed that the LTA+80 effect was much stronger in young individuals. In the combined sample of 298 Vietnamese familial trios, the odds ratio of leprosy for LTA+80 AA/AC versus CC subjects was 2.11 ($P = 0.000024$), which increased to 5.63 ($P = 0.0000004$) in the subsample of 121 trios of affected individuals diagnosed before 16 years of age. In addition to identifying LTA as a major gene associated with early-onset leprosy, our study highlights the critical role of case- and population-specific factors in the dissection of susceptibility variants in complex diseases.

Singh M, Balamurugan A, Katoch K, Sharma SK, Mehra NK. Immunogenetics of mycobacterial infections in the North Indian population. *Tissue Antigens* 2007; 69 Suppl 1: 228-30.

Several lines of evidence highlight the genetic basis of risk to develop mycobacterial diseases. Human leukocyte antigen (HLA)-DR2 alleles (DRB1*1501 and DRB1*1502) have been found to be strongly associated with mycobacterial disease, especially the more severe forms such as lepromatous leprosy and multidrug-resistant pulmonary tuberculosis. In this study, DNA-based high-resolution typing techniques of polymerase chain reaction-sequence-specific oligonucleotide probe were used to determine the distribution of HLA-DR/DQ alleles in patients with leprosy and pulmonary tuberculosis. Analysis of different DR2 subtypes based on valine/glycine dimorphism at codon beta86 in pocket 1 of HLA-DR showed an inverse relationship of DR2 alleles with V/G as the severity of disease increased both in leprosy and in pulmonary tuberculosis.

Souza FC, Marcos EV, Ura S, Opromolla PA, Nogueira ME. Estudo comparativo entre reação de Mitsuda e antígenos leucocitários humanos em pacientes hansenianos. *Rev Soc Bras Med Trop* 2007; 40(2): 188-91.

In this study, we aimed to compare the Mitsuda skin test with the alleles HLA-DR2/HLA-DR3 and HLA-DQ1, in relation to the clinical forms of leprosy in 176 patients (50 TT, 50 LL and 76 B). The results obtained did not reveal any association between the Mitsuda reaction and the HLA alleles in the clinical forms isolated. However, when analyzed according to Mitsuda test response, a significant association was found between patients with negative Mitsuda reaction and HLA-DQ1 ($p=0.002$). No association was observed between positive Mitsuda reaction and the HLA-DR2/DR3 alleles. We concluded that the allele HLA-DQ1 has an important participation when there is no response to the Mitsuda test. We suggest that more specific studies should be developed on this allele.

Sato N, Fujimura T, Masuzawa M, Yogi Y, Matsuoka M, Kanoh M, Riley LW, Katsuoka K. Recombinant *Mycobacterium leprae* protein associated with entry into mammalian cells of respiratory and skin components. *J Dermatol Sci* 2007; 46(2): 101-10.

BACKGROUNDS: The transmission of *Mycobacterium leprae*, the causative pathogen of leprosy, has been postulated to occur mainly through upper respiratory route rather than skin-to-skin contact via minor injuries. The *M. leprae* genome contains *mce1A* gene, which encodes a putative mammalian cell entry protein. However, to date, there have been no functional analyses of the *M. leprae* *mce1A* gene product. **OBJECTIVE:** The aim of this study was to elucidate a possible relationship between this transmission mechanism and the *mce1A* gene product. **METHODS:** We analyzed the cell uptake activity in vitro of polystyrene latex beads coated with a purified recombinant (r-) protein expressed by a 849-bp locus within the *mce1A* gene. **RESULTS:** The r-protein promoted uptake of the beads into human nasal epithelial cells derived from nasal polyps, human bronchial epithelial cell line, normal human dermal fibroblasts, normal human microvascular endothelial cells and normal human keratinocytes cultured at 0.01 mM extracellular calcium concentration [Ca]; no uptake occurred with keratinocytes cultured at 1.2mM [Ca]. **CONCLUSION:** These results suggest that the *mce1A* gene product can mediate *M. leprae* entry into respiratory epithelial cells as their natural target cells, which may be the main mode of transmission. Endothelial cells, on the other hand, may serve as the reservoir of the bacilli for long-term infection. The *M. leprae* *Mce1A* protein has potential important implications for mode of transmission and pathogenesis of leprosy.

Johnson CM, Traherne JA, Jamieson SE, Tremelling M, Bingham S, Parkes M, Blackwell JM, Trowsdale J. Analysis of the BTNL2 truncating splice site mutation in tuberculosis, leprosy and Crohn's disease. *Tissue Antigens* 2007; 69(3): 236-41.

The region on chromosome 6 encoding the major histocompatibility complex (MHC) is associated with a number of autoimmune and infectious diseases. Primary susceptibility to many of these has been localized to a region containing the human leukocyte antigen (HLA)-DR and -DQ genes. A recent study of sarcoidosis has provided evidence of an independent effect, associated with a truncating single nucleotide polymorphism (SNP) of a nearby gene, BTNL2. This gene may encode an immune receptor involved in costimulation. Sarcoidosis, tuberculoid leprosy, tuberculosis (TB) and Crohn's disease all have similar immunological features, including a Th1 response with granuloma formation. In addition mycobacteria have been identified or suggested to be causative pathogens in such conditions. We genotyped the truncating BTNL2 SNP in 92 TB and 72 leprosy families from Brazil and carried out family-based association studies. We could not find evidence of overtransmission of the truncating allele in TB. There was an association with susceptibility to leprosy ($P=0.04$), however, this is most likely due to linkage disequilibrium with HLA-DR. We also genotyped 476 UK Caucasian cases of Crohn's disease with 760 geographically matched controls and found no evidence of a disease association. We conclude that the truncating BTNL2 SNP is not important in this group of Th1 dominated granulomatous diseases.

Literatura corrente em hanseníase

Weng X, Wang Z, Liu J, Kimura M, Black WC, Brennan PJ, Li H, Vissa VD. Identification and distribution of *Mycobacterium leprae* genotypes in a region of high leprosy prevalence in China: a 3-year molecular epidemiological study. *J Clin Microbiol* 2007; 45(6): 1728-34.

Multiple-locus variable-number tandem-repeat (VNTR) analysis (MLVA) has been proposed as a means of strain typing for tracking the transmission of leprosy. However, empirical data for a defined population are lacking. To this end, a study was initiated to assess the diversity and distribution of prevalent *Mycobacterium leprae* strains in Qiubei County, Yunnan Province, People's Republic of China, where the annual detection rate of leprosy is 10-fold higher than the national average rate. Sixty-eight newly diagnosed leprosy patients were included in the study. MLVA at eight *M. leprae* loci was applied using DNA extracts from skin biopsies. The number of alleles per locus ranged from 4 to 24, providing adequate strain discrimination. MLVA strain typing identified several clusters of patients whose *M. leprae* specimens shared similar VNTR profiles. Two of these clusters were comprised of patients who resided predominantly in the north and northwest parts of Qiubei County. Furthermore, it was found that multicase families are common in this county: 23 of the 68 patients were from 11 families. Intrafamilial VNTR profiles closely matched within six families, although they were different between the families. Moreover, VNTR patterns related to those found in some multicase families were also detected in patients in the same or adjacent townships, indicating the utility of VNTR strain typing to identify and detect short-range transmission events. Social contact through village markets is proposed as a means of transmission.

Johnson CM, Lyle EA, Omueti KO, Stepensky VA, Yegin O, Alpsoy E, Hamann L, Schumann RR, Tapping RI. Cutting edge: a common polymorphism impairs cell surface trafficking and functional responses of TLR1 but protects against leprosy. *J Immunol* 2007; 178(12): 7520-4.

TLRs constitute an essential family of pattern recognition molecules that, through direct recognition of conserved microbial components, initiate inflammatory responses following infection. In this role, TLR1 enables host responses to a variety of bacteria, including pathogenic species of mycobacteria. In this study, we report that I602S, a common single nucleotide polymorphism within TLR1, is associated with aberrant trafficking of the receptor to the cell surface and diminished responses of blood monocytes to bacterial agonists. When expressed in heterologous systems, the TLR1 602S variant, but not the TLR1 602I variant, exhibits the expected deficiencies in trafficking and responsiveness. Among white Europeans, the 602S allele represents the most common single nucleotide polymorphism affecting TLR function identified to date. Surprisingly, the 602S allele is associated with a decreased incidence of leprosy, suggesting that *Mycobacterium leprae* subverts the TLR system as a mechanism of immune evasion.

Vanderborght PR, Pacheco AG, Moraes ME, Antoni G, Romero M, Verville A, Thai VH, Huong NT, Ba NN, Schurr E, Sarno EM, Moraes MO. HLA-DRB1*04 and DRB1*10 are associated with resistance and susceptibility, respectively, in Brazilian and Vietnamese leprosy patients. *Genes Immun* 2007; 8(4): 320-4

The host genetic background has been considered one of the factors that influence leprosy outcome, a chronic infectious disease caused by *Mycobacterium leprae*. Genome scans demonstrated that the 6p21 region is associated with leprosy and a substantial number of population-based studies analyzing human leukocyte antigen (HLA) class II loci suggested association of HLA-DR with leprosy. However, some studies lacked robustness as they had limited power. Indeed, experimental designs require increased sample size to achieve adequate power, as well as replication studies with independent samples for confirmation of previous findings. In this work, we analyzed the influence of the HLA-DRB1 locus on leprosy susceptibility per se and disease type using a case-control design carried out in Brazilians (578 cases and 691 controls) and a replication study based on a family design in a Vietnamese population (n=194 families). The results showed that HLA-DRB1*10 is associated with susceptibility to leprosy and HLA-DRB1*04 is associated with resistance, both in the Brazilian and Vietnamese populations suggesting that these alleles play an important role in the activation of cellular immune responses against *M. leprae*.

Vejbaesya S, Mahaisavariya P, Luangtrakool P, Sermduangprateep C. TNF alpha and NRAMP1 polymorphisms in leprosy. *J Med Assoc Thai* 2007; 90(6): 1188-92.

OBJECTIVE: To determine the association of TNF alpha and NRAMP1 polymorphisms in leprosy. **MATERIAL AND METHOD:** The polymorphisms of TNF alpha at -238, -308, and NRAMP1 at INT4, D543N, and 3' UTR were examined in 37 patients with leprosy (24 multibacillary and 13 paucibacillary) and 140 healthy controls. PCR-SSP and PCR-SSO method were used to type TNF and NRAMP1 polymorphisms. **RESULTS:** The genotype frequency of TNF-308 G/A was significantly increased in all leprosy patients compared to the controls ($p = 0.04$, OR = 2.69). When leprosy types were divided, the allele frequency of TNF-308A was significantly increased in multibacillary leprosy compared to the normal controls ($p = 0.04$, OR = 2.93). There was no significant difference in the distribution of the genotypes and allele frequencies of TNF -238 and NRAMP1 polymorphisms between the patients and controls. **CONCLUSION:** TNF-308A was associated with susceptibility to multibacillary leprosy.

HANSENÍASE EXPERIMENTAL

Noon LA, Lloyd AC. Treating leprosy: an Erb-al remedy?. *Trends Pharmacol Sci* 2007; 28(3): 103-5.

The leprosy pathogen *Mycobacterium leprae* attacks Schwann cells in the peripheral nervous system, causing them to demyelinate. Recent work by Tapinos et al. shows that a direct mechanism of demyelination induced by *M. leprae* depends on the binding of the bacterium to the receptor tyrosine kinase ErbB2 on Schwann cells and the resulting activation of the Ras-Raf-MEK-ERK pathway. These findings have relevance for the potential treatment of leprosy and they highlight parallels between the dedifferentiation signal in leprosy and that in nerve injury and cancer.

Matrat S, Petrella S, Cambau E, Sougakoff W, Jarlier V, Aubry A. Expression and purification of an active form of the *Mycobacterium leprae* DNA gyrase and its inhibition by quinolones. *Antimicrob Agents Chemother* 2007; 51(5): 1643-8

Mycobacterium leprae, the causative agent of leprosy, is noncultivable in vitro; therefore, evaluation of antibiotic activity against *M. leprae* relies mainly upon the mouse footpad system, which requires at least 12 months before the results become available. We have developed an in vitro assay for studying the activities of quinolones against the DNA gyrase of *M. leprae*. We overexpressed in *Escherichia coli* the *M. leprae* GyrA and GyrB subunits separately as His-tagged proteins by using a pET plasmid carrying the *gyrA* and *gyrB* genes. The soluble 97.5-kDa GyrA and 74.5-kDa GyrB subunits were purified by nickel chelate chromatography and were reconstituted as an enzyme with DNA supercoiling activity. Based on the drug concentrations that inhibited DNA supercoiling by 50% or that induced DNA cleavage by 25%, the 13 quinolones tested clustered into three groups. Analysis of the quinolone structure-activity relationship demonstrates that the most active quinolones against *M. leprae* DNA gyrase share the following structural features: a substituted carbon at position 8, a cyclopropyl substituent at N-1, a fluorine at C-6, and a substituent ring at C-7. We conclude that the assays based on DNA supercoiling inhibition and drug-induced DNA cleavage on purified *M. leprae* DNA gyrase are rapid, efficient, and safe methods for the screening of quinolone derivatives with potential in vivo activities against *M. leprae*.

Wek-Rodriguez K, Silva-Miranda M, Arce-Paredes P, Rojas-Espinosa O. Effect of reactive oxygen intermediaries on the viability and infectivity of *Mycobacterium lepraemurium*. *Int J Exp Pathol* 2007; 88(3): 137-45.

Murine leprosy is a natural disease of the mouse, the most popular model animal used in biomedical research; the disease is caused by *Mycobacterium lepraemurium* (MLM), a successful parasite of macrophages. The aim of the study was to test the hypothesis that MLM survives within macrophages because it highly resists the toxic effects of the reactive oxygen intermediaries produced by these cells in response to infection by the microorganism. MLM cells were incubated in the presence of horseradish peroxidase (HRPO)-H₂O₂-halide for several periods of time. The peroxidative effect of this system was investigated by assessing the changes occurred in (a) lipid composition; (b) viability; and (c) infectivity of the microorganism. Changes in the lipid composition of peroxidated- vs. intact-MLM were analysed by thin layer chromatography. The effect of the peroxidative system on the viability and infectivity of MLM was measured by the alamar blue reduction assay and by its ability to produce an infection in the mouse, respectively. Peroxidation of MLM produced drastic changes in the lipid envelope of the microorganism, killed the bacteria and abolished their ability to produce an in vivo infection in the mouse. In vitro, MLM is highly susceptible to the noxious effects of the HRPO-H₂O₂-halide system. Although the lipid envelope of MLM might protect the microorganism from the peroxidative substances produced at 'physiological' concentrations in vivo, the success of MLM as a parasite of macrophages might rather obey for other reasons. The ability of MLM to enter macrophages without triggering these cells' oxidative response and the lack of granular MPO in mature macrophages might better explain its success as an intracellular parasite of these cells.

Courtin F, Huerre M, Fyfe J, Dumas P, Boschioli ML. A case of feline leprosy caused by *Mycobacterium lepraemurium* originating from the island of Kythira (Greece): diagnosis and treatment. *J Feline Med Surg* 2007; 9(3): 238-41.

A 2-year-old, 4 kg, healthy, domestic shorthair female cat presented with ulcerated subcutaneous nodules on the commissures of its mouth. The cat was negative for feline leukaemia virus and feline immunodeficiency virus. Skin mycobacteriosis was diagnosed after detection of numerous acid-fast bacilli in Ziehl Neelsen-stained smears from the ulcers. Feline leprosy was suspected following preliminary polymerase chain reaction results: positive for *Mycobacterium* genus but negative for *Mycobacterium tuberculosis* and *Mycobacterium avium* complexes. *Mycobacterium lepraemurium* was later identified following DNA sequence analysis of the 5' end of the 16S rRNA gene and the 16S-23S internal transcribed spacer region. Microscopic lesions consisted of pyogranulomas containing mainly large foamy macrophages with 10- 100 intracellular acid-fast bacilli per field. The cat was cured after surgery and a 14-week course of clofazimine (30 mg daily) and clarithromycin (50 mg twice daily).

HISTÓRIA

185 - Mori S, Ishii N. Leprosy and medicine II--progress and establishment of an absolute isolation policy. *Nihon Hansenbyo Gakkai Zasshi* 2007; 76(1): 29-65.

The leprosy policy of Japan began from when the government enacted [quot]law No. 11 (The leprosy prevention act)[quot] in 1907 (Meiji 40) and several leprosy sanatoriums were built to receive previously homeless patients. Then, with the rise of totalitarianism, the isolation policy of Japan gained national support under the slogan [quot]Patient Relief[quot], which would become a major factor behind the enactment of [quot]Leprosy Prevention Law[quot] in 1931 (Showa 6) by which the leprosy policy was changed to one of absolute isolation aimed at the internment of all leprosy patients. From recent research on the leprosy policy of Japan, the internment of all leprosy patients, isolation for life, social defense, and neglect of patients' human-rights had tragic results in many cases. However, there is little research which can reply clearly to the question of whether the leprosy policy of Japan was really original and what factors led to the formation of the absolute isolation policy. This paper focuses on the relation between leprosy policy and treatment, and from this, I make clear the similarities, or peculiarities, of the isolation policy between Japan and the rest of the world, while clarifying the factors associated with the progress of the absolute isolation policy. The processes involved were historical and medical historical in that the relation between the formation of a national health system and the progress of the isolation policy of Meiji Era, the proposal of the isolation policy by Dr. Keizo Dohi, Dr. Shibasaburo Kitasato, and Dr. Masatsugu Yamane; the practical application of this policy by Dr. Kensuke Mitsuda, and the decision to enact this policy and its support by the Health and Medical Bureau and the Department of the Interior, as well as many other factors, all contributed to the final implementation of the absolute isolation policy.

Menke HE, Wille RJ, Faber WR, Pieters T. Bijdragen van Nederland en zijn koloniën aan de kennis over de oorzaak van lepra in de 19e eeuw. *Ned Tijdschr Geneesk* 2007; 151(14): 825-30.

OBJECTIVE: To determine the Dutch contributions to the formulation of the concept that leprosy is an infectious disease. DESIGN: Literature study. METHOD: A search for relevant publications was made in the *Nederlands Tijdschrift voor Geneeskunde* (Dutch journal of Medicine; NTvG) and the *Geneeskundig Tijdschrift voor Nederlandsch-Indië* (Medical Journal of the Dutch Indies; GTNI) with the aid of the search terms 'lepra [leprosy]', 'lepra Arabum [Arab leprosy]', 'melaatsheid [leprosy]' and 'elephantiasis Graecorum [Greek elephantiasis]'. In addition, on the basis of references in the publications in the NTvG and the GTNI, as well as via searches in the catalogues of the Royal Library in The Hague and the libraries of Dutch universities, an inventory was made of the Dutch medical dissertations and other monographs on leprosy, as well as the medical historical review articles, from the 19th century. RESULTS: For a long time, physicians described the aetiology of leprosy in terms of 'a substrate' to which all sorts of mixtures of infection, heredity and hygiene contributed. From the middle of the 19th century onwards, this explanatory model with multiple possible solutions gave way to a controversy between two explanatory models: heredity as an 'anti-contagious' principle versus contagiousity. These two explanatory models were mutually exclusive in their universal aspirations. The debate in the Netherlands took place in the field of tension between European concepts on the one hand and on the other hand ideas and practices resulting from the interaction between the Netherlands and its colonies. Inspired in part by the writings of the Dutch physician C L Drognat Landré, who based his contagion theory on observations in Surinam, the Norwegian G. H. A. Hansen discovered the leprosy bacillus in 1873. It was not until 1897, at the international leprosy conference in Berlin, however, that consensus was to be reached on leprosy being an infectious disease. CONCLUSION: An essential contribution to the development of the

contemporary ideas as to the cause of leprosy was made from the Netherlands.

Ryan TJ. Community dermatology inclusive of leprosy: its past present and future. *Lepr Rev* 2007; 78(1): 7-10.

The archives of leprosy and its global history are currently evolving in Oxford. A collection of documents and books are housed in the historical library of Sir William Osler under the heading of 'Public Health before and after Osler' and the history of leprosy can be found on <http://www.leprosyhistory.org>. A striking feature of the old books is their attention to the designation 'Lepra' and the evolution of not just leprosy but of the other differential diagnoses of the eighteenth and nineteenth century such as psoriasis. Even in the twentieth century, the development of a major interest in Oxford led by Weddell was the innervation of the skin first in psoriasis and then in leprosy, joint meetings with Weddell, Cochrane, Browne, Rees and others over patients with leprosy, to the building of the Cochrane Annex and the work of Colin MacDougal in the Department of Dermatology.

Appelboom T, Cogan E, Klastersky J. Job of the Bible: leprosy or scabies? *Mt Sinai J Med* 2007; 74(1): 36-9.

Proposing a medical diagnosis a posteriori of a person who died a long time ago is not as impossible as it sounds if sufficient medical history is available. A whole book of the Bible is devoted to Job and his trials. The diagnosis of leprosy has been generally accepted by medieval commentators because the verses of the Book speak of ulcers disseminated over the skin, and also because leprosy is an exemplary sanction imposed by way of example by God to punish those who have committed a sin. In this paper, we have taken the different verses with a medical content from the Book of Job, and reconstructed the clinical picture as if the patient had turned up in the 21st century in order to see if the diagnosis of leprosy may be called into question, and to discuss the limits of the medico-historic approach. The clinical picture of the disease consists of deterioration in the general condition, with widespread pain, confusion, skin eruptions, bilious vomiting, and so on. Under these conditions, if Job did exist, and if the retrospective medical history is reliable, the most likely diagnosis is that of scabies rather than leprosy.

Literatura corrente em hanseníase

IMUNOLOGIA

Sabet S, Choa MT, Sieling PA, Rea TH, Modlin RL. Functional characterization of a T-cell receptor BV6+ T-cell clone derived from a leprosy lesion. *Immunology* 2007; 120(3): 354-61.

Human infection with *Mycobacterium leprae*, an intracellular bacterium, presents as a clinical and immunological spectrum; thus leprosy provides an opportunity to investigate mechanisms of T-cell responsiveness to a microbial pathogen. Analysis of the T-cell receptor (TCR) repertoire in leprosy lesions revealed that TCR BV6(+) T cells containing a conserved CDR3 motif are over-represented in lesions from patients with the localized form of the disease. Here, we derived a T-cell clone from a leprosy lesion that expressed TCR BV6 and the conserved CDR3 sequence L-S-G. This T-cell clone produced a T helper type 1 cytokine pattern, directly lysed *M. leprae*-pulsed antigen-presenting cells by the granule exocytosis pathway, and expressed the antimicrobial protein granulysin. BV6(+) T cells may therefore functionally contribute to the cell-mediated immune response against *M. leprae*.

Edington FL, Bacellar MO, Machado PR, Barbosa L, Reis E, Reis M, Santiago MB. Anti-neutrophil cytoplasmic antibodies in leprosy. *Clin Rheumatol* 2007; 26(2): 208-10.

INTRODUCTION: Anti-Neutrophil Cytoplasmic Antibodies (ANCA) are auto-antibodies directed to intracellular components of neutrophils and used to be considered as present almost exclusively in granulomatous vasculitis. Recently, these auto-antibodies have been found in other autoimmune disorders as well as infectious diseases. **MATERIALS AND METHODS:** We studied patients with leprosy confirmed by bacilloscopy and/or skin biopsy, in reaction phase from the Ambulatório de Hanseníase do Hospital Universitário Professor Edgar Santos. ANCA and Antinuclear antibodies (ANA) were determined by indirect immunofluorescence using commercially available kits. **RESULTS:** Twenty patients were enrolled in our study, nine males and 11 females. The mean age was 36.9±18.2 years. ANCA were present only in one patient, with a perinuclear staining pattern (p-ANCA), and no patient tested positive for ANA. **DISCUSSION:** Although other studies have shown the presence of ANCA in leprosy, the low frequency of these antibodies in leprosy sera demonstrated in the present study illustrates the high specificity of ANCA for the diagnosis of Wegener granulomatosis.

Murray RA, Siddiqui MR, Mendillo M, Krahenbuhl J, Kaplan G. Mycobacterium leprae inhibits dendritic cell activation and maturation. *J Immunol* 2007; 178(1): 338-44.

Leprosy presents with a clinical spectrum of skin lesions that span from strong Th1-mediated cellular immunity and control of bacillary growth at one pole to poor Ag-specific T cell immunity with extensive bacillary load and Th2 cytokine-expressing lesions at the other. To understand how the immune response to Mycobacterium leprae is regulated, human dendritic cells (DC), potent inducers of adaptive immune responses, exposed to M. leprae, Mycobacterium tuberculosis (Mtb), and Mycobacterium bovis bacillus Calmette-Guerin (BCG) were studied for their ability to be activated and to prime T cell proliferation. In contrast with Mtb and BCG, M. leprae did not induce DC activation/maturation as measured by the expression of selected surface markers and proinflammatory cytokine production. In MLR, T cells did not proliferate in response to M. leprae-stimulated DC. Interestingly, M. leprae-exposed MLR cells secreted increased Th2 cytokines as well as similar Th1 cytokine levels as compared with Mtb- and BCG-exposed cells. Gene expression analysis revealed a reduction in levels of mRNA of DC activation and maturation markers following exposure to M. leprae. Our data suggest that M. leprae does not induce and probably suppresses in vitro DC maturation/activation, whereas Mtb and BCG are stimulatory.

Finiasz MR, Franco MC, Barrera S, Rutitzky L, Pizzariello G, Carmen Sasiain M, Renauld JC, Van Snick J, Fink S. IL-9 promotes anti-Mycobacterium leprae cytotoxicity: involvement of IFN γ . *Clin Exp Immunol* 2007; 147(1): 139-47.

Interleukin 9 (IL-9) is a T-cell derived factor preferentially expressed by CD4⁺ Th2 cells and it has been characterized both in human and murine systems. It is a pleiotropic cytokine with multiple functions on cells of the lymphoid, myeloid and mast cell lineages, as well as on lung epithelial cells. Other activities described for IL-9 support its contribution to asthma and its important role in helminthic infections, where a Th2 response can be protective and IL-9 enhances resistance or is responsible for elimination of the nematode. Nevertheless, until recently there were no studies on its role in bacterial infections in man. We have demonstrated that cytokines can modulate the specific cytotoxicity generation in peripheral blood mononuclear cells from leprosy patients and normal controls. In the present report we studied the effect of IL-9 in this experimental model. Our results indicate that IL-9 can counteract the negative effect mediated by IL-4 on the generation of M. leprae-induced cytotoxic T lymphocytes. Moreover, it can increase this lytic activity in controls and enhance the stimulatory effect of IL-2 or IL-6 in cells from leprosy patients and controls. IL-9 is also able to revert the inhibitory effect of IL-10 and IL-13 on the M. leprae-induced cytotoxic activity. Although the exact mechanism of action of IL-9 remains to be determined, interferon gamma seems to be required for the effect of IL-9 in this experimental model. These data suggest that IL-9 may have an atypical Th2 behaviour and play a role in the modulation of the immune response to mycobacterial infections.

Literatura corrente em hanseníase

Parkash O, Pandey R, Kumar A, Kumar A. Performance of recombinant ESAT-6 antigen (ML0049) for detection of leprosy patients. *Lett Appl Microbiol* 2007; 44(5): 524-30.

AIMS: The study was aimed to evaluate the *Mycobacterium leprae* recombinant early secreted antigenic target-6 (rESAT-6) for its serological performance in leprosy patients. **METHODS AND RESULTS:** Employing enzyme-linked immunosorbent assay (ELISA), serum samples were tested for prevalence of immunoglobulin G antibodies against *M. leprae* rESAT-6. The results revealed that the sensitivity of the assay for smear-positive leprosy patients was 82.4% (14 of 17) while for smear-negative patients it was 19.4% (six of 31). Interestingly, the performance of ESAT-6-based assay was statistically comparable with anti-phenolic glycolipid-I antibody-detecting ELISA, a most widely studied serological assay in leprosy. Regarding specificity, none of the 48 controls was positive indicating that antibody response to ESAT-6 was highly specific. Moreover, a high concordance between bacterial index and anti-ESAT-6 antibody-detecting assay was noted. **CONCLUSIONS:** Recombinant ESAT-6 seems to be a potential serological reagent for detection of *M. leprae* infection. **SIGNIFICANCE AND IMPACT OF THE STUDY:** ESAT-6 serology may have utility for (i) early diagnosis, particularly, of highly infectious form (multibacillary, MB) of leprosy, (ii) monitoring the response in smear-positive leprosy patients during the course of the chemotherapy, (iii) classification of leprosy patients into MB and paucibacillary groups for treatment purpose. Hence, further research on these lines is warranted.

Fulco TO, Lopes UG, Sarno EM, Sampaio EP, Saliba AM. The proteasome function is required for *Mycobacterium leprae*-induced apoptosis and cytokine secretion. *Immunol Lett* 2007; 110(1): 82-5.

Previous studies have demonstrated the importance of the ubiquitin-proteasome pathway in the immune response to bacterial pathogens. To investigate the role of this system in the context of leprosy, *Mycobacterium leprae*-stimulated peripheral blood mononuclear cells (PBMC) were treated with the proteasome inhibitor MG132 to assess the levels of apoptosis and cytokine secretion. The results showed that the inhibition of proteasome activity significantly reduced *M. leprae*-mediated cell death. In addition, MG132 treatment led to a significant decrease in *M. leprae*-induced TNF-alpha and IL-10 secretion. Together, these results suggest that modulations of the ubiquitin-proteasome pathway may participate in the human response to *M. leprae*.

Maeda Y, Mukai T, Kai M, Fukutomi Y, Nomaguchi H, Abe C, Kobayashi K, Kitada S, Maekura R, Yano I, Ishii N, Mori T, Makino M. Evaluation of major membrane protein-II as a tool for serodiagnosis of leprosy. *FEMS Microbiol Lett* 2007; 272(2): 202-5.

As serodiagnosis is the easiest way of diagnosing a disease, the utility of *Mycobacterium leprae*-derived major membrane protein-II (MMP-II), one of the immuno-dominant antigens, in the serodiagnosis of leprosy was examined. The percent positivity by an enzyme-linked immunosorbent assay for anti-MMP-II antibody was 82.4% for multi-bacillary leprosy, and the specificity of the test was 90.1%. For paucibacillary leprosy where cell-mediated immunity predominates, 39.0% showed positive results. These percentage values were significantly higher than these values obtained for existing phenolic glycolipid-I based methods, suggesting that MMP-II antibody detection would facilitate the diagnosis of leprosy.

Sieling PA, Legaspi A, Ochoa MT, Rea TH, Modlin RL. Regulation of human T-cell homing receptor expression in cutaneous bacterial infection. *Immunology* 2007; 120(4): 518-25.

We investigated the regulation of T-cell homing receptors in infectious disease by evaluating the cutaneous lymphocyte antigen (CLA) in human leprosy. We found that CLA-positive cells were enriched in the infectious lesions associated with restricting the growth of the pathogen *Mycobacterium leprae*, as assessed by the clinical course of infection. Moreover, CLA expression on T cells isolated from the peripheral blood of antigen-responsive tuberculoid leprosy patients increased in the presence of *M. leprae* (2.4-fold median increase; range 0.8-6.1, n = 17), but not in unresponsive lepromatous leprosy patients (1.0-fold median increase; range 0.1-2.2, n = 10; P < 0.005). *Mycobacterium leprae* specifically up-regulated the skin homing receptor, CLA, but not alpha(4)/beta(7), the intestinal homing receptor, which decreased on T cells of patients with tuberculoid leprosy after antigen stimulation (2.2-fold median decrease; range 1.6-3.4, n = 3). Our data indicate that CLA expression is regulated during the course of leprosy infection and suggest that T-cell responsiveness to a microbial antigen directs antigen-specific T cells to the site of infection.

Morahan G, Kaur G, Singh M, Rapthap CC, Kumar N, Katoch K, Mehra NK, Huang D. Association of variants in the IL12B gene with leprosy and tuberculosis. *Tissue Antigens* 2007; 69 Suppl 1: 234-6.

There is a great range in outcomes after mycobacterial infections, and this is probably due to individual variation in immune responses. One of the key cytokine regulators of the immune response is interleukin (IL-) 12. The IL12B gene encodes the p40 chain of both IL-12 and IL-23 and it has two major variant sites at which different alleles are associated with increased levels of gene expression and with susceptibility to a range of immune-related diseases. We hypothesized that IL12B variants associated with increased expression would be as associated with susceptibility to persistent mycobacterial infection. We tested this hypothesis by genotyping Indian subjects, having either leprosy or tuberculosis (TB), as well as ethnically matched controls. Subjects with leprosy were less likely to have the 3'UT R genotype associated with lower IL12B expression (P= 0.001). Subjects with TB were not only more likely to have the high-expressing IL12B promoter genotype (P= 0.01) but also more likely to have this in the same haplotype with the high expressing 3'UTR allele (P= 0.0009). These results suggest these infectious diseases may be improved by modulating IL-12p40 production.

Literatura corrente em hanseníase

Chaturvedi V, Girdhar BK, Sengupta U, Sinha S. Semi-quantitative detection of *Mycobacterium leprae* antigens in skin scrapings: suitability as a laboratory aid for field diagnosis of leprosy. *Trans R Soc Trop Med Hyg* 2007; 101(7): 699-706.

We describe here a method, potentially suitable for field applications, for semi-quantitative detection of *Mycobacterium leprae* antigens in skin scrapings, which are taken normally for smear microscopy. Thirty acid-fast bacilli-negative paucibacillary (PB) leprosy patients comprised the main study group; eight acid-fast bacilli-positive multibacillary (MB) patients and five healthy laboratory workers served as controls. Samples in saline were spotted on nitrocellulose paper and probed with mycobacterium-specific polyclonal or *M. leprae*-specific mAbs against 12, 35 and 65kDa protein antigens, using a dot-ELISA format. Spot densities were read through a densitometer and also graded visually. The polyclonal antibody produced the best sensitivity, resulting in densitometric detection of mycobacterial antigen in 100% MB, 76% multiple-lesion PB and 62% single-lesion PB patients. None of the healthy volunteers showed antigen positivity. A correlation was noted between the densitometric and visual estimates of the antigen. Determination of antigen in the lesion and an apparently uninvolved area of skin in a subset of PB patients provided clues to the state of the underlying infection. Serological positivity of PB patients for *M. leprae*-specific antibodies against the 35kDa and phenolic glycolipid-I antigens was too low (<20%) for any diagnostic significance.

MICROBIOLOGIA

Marsollier L, André JP, Frigui W, Reysset G, Milon G, Carbonnelle B, Aubry J, Cole ST. Early trafficking events of *Mycobacterium ulcerans* within *Naucoris cimicoides*. *Cell Microbiol* 2007; 9(2): 347-55.

The severe skin-destructive disease caused by *Mycobacterium ulcerans*, named Buruli ulcer, is the third most important mycobacterial disease in humans after tuberculosis and leprosy. Recently we demonstrated that *M. ulcerans* could colonize the salivary glands of the water bug, *Naucoris cimicoides*. In this study, we report that *M. ulcerans* may be delivered from the digested prey aspirate to the coelomic cavity via a unique headspace, the head capsule (HC). During the infected meal, we observed that *M. ulcerans* clusters adhered to the stylets that were retracted in the HC at the end of the meal. *M. ulcerans* was able to translocate from the HC to the coelomic cavity where it is phagocytosed by the plasmatocytes. These cells are subverted as shuttle cells and deliver *M. ulcerans* to the salivary glands. At this early stage of its parasitic life style, two other important features of *M. ulcerans* can be documented: first, mycolactone is not required for translocation of *M. ulcerans* into the HC, in contrast to the next step, colonization of the salivary glands; second, *M. ulcerans* clusters bind a member of the serpin protein family present in the salivary gland homogenate.

ussain T. Leprosy and tuberculosis: an insight-review. Crit Rev Microbiol 2007; 33(1): 15-66.

A quick glance at this review article provides an insight into the common and different features of *M. leprae* and *M. tuberculosis* and the diseases caused by these organisms. Table I provides the popular names, history, stigma, description of the disease, clinical features, classification and the types of disease manifestations, who are affected, Signs and Symptoms, Clinical examination, treatment regimens, reactions, relapses, immunity, infectiousness, risk groups, deformities, sequelae, transmission, prevention, complications, vaccination, laboratory studies, days of importance for both the diseases. Table II provides information regarding the causative organisms, *M. leprae* and *M. tuberculosis*, their size, genome, protein coding region, lost genes, pseudogenes, classification, predilection, incubation period, ecology, cell structure, metabolism, resistance, bacterial index, growth in vitro, experimental animals, etc. Table III provides figures of *M. leprae* and *M. tuberculosis*, their genome, Lepromin and Tuberculin testing, Global scenario, Indian scenario, colonies of *M. leprae* and *M. tuberculosis*, drugs for treatment of tuberculosis and leprosy (MDT blister pack), and so on.

OFTALMOLOGIA

Torres-Larrosa MT, Pérez-Pérez LJ, Quintana Ginestar MV, Torres-Peris V, Artazkoz del Toro JJ. Lepra nasal: impacto de la multiterapia en la morfología y la fisiología nasal. Acta Otorrinolaringol Esp 2007; 58(5): 182-6.

INTRODUCTION: The multi-drug therapy protocol has allowed leprosy patients following this strategy to achieve complete recovery without developing neurotrophic sequelae or deformities. **OBJECTIVES:** To assess the impact of multi-drug therapy on the development of nasal deformities and nasal airway patency. **PATIENTS AND METHOD:** In an overall group of 84 patients studied, 38 were treated with a therapy based on a single drug and 22 were treated with multi-drug while 24 subjects formed a control group. Nose morphology was determined by anterior rhinoscopy. Nasal patency and flow resistances were measured by anterior rhinomanometry. The results were compared by using the Anova test for a single variable. **RESULTS:** The nasal structures in the group with therapy based on a single drug underwent resorption of bone and cartilage in the structures of the nose and increased flow resistance. In the group receiving the multi-drug protocol, there were no significant morphological alterations and nasal patency and flow resistance remained within normal levels. **CONCLUSIONS:** The multi-drug therapy is effective in preventing the development of nasal deformities and maintains normal nasal airflow.

Literatura corrente em hanseníase

Millar MJ, Bulliard C, Balachandran C, Maloof AJ. Mycobacterium hemophilum infection presenting as filamentary keratopathy in an immunocompromised adult. *Cornea* 2007; 26(6): 764-6.

To report a case of Mycobacterium hemophilum of the eye. **METHODS:** Case report with pathologic correlation. A 55-year-old Malaysian man with a 3-year history of graft-versus-host disease presented with dry eye and keratopathy. **RESULTS:** The diagnosis was not initially evident, despite biopsy specimens of the conjunctiva. Definitive diagnosis was made after dermatology consultation suggested a histoid variant of lepromatous leprosy, prompting Ziehl-Neelsen staining of the initial and subsequent conjunctival biopsies with subsequent polymerase chain reaction testing. Anti-M. hemophilum treatment resulted in prompt resolution of ocular signs. **CONCLUSIONS:** Mycobacterium hemophilum is a rare condition, affecting mainly immunocompromised patients. Although filamentary keratopathy has been described as common manifestations of leprosy, to date, no ocular manifestations of M. hemophilum have been described. Conjoint management with infectious disease and clinical microbiology is imperative to ensure accurate diagnosis and appropriate early intervention. The effect of systemic immunosuppression is relevant in such patients.

PATOLOGIA

Fleury RN, Duerksen F. Emergency in leprosy: involvement of the larynx. *Lepr Rev* 2007; 78(2): 148-50

We present eight patients with larynx involvement in leprosy. Seven were classified as lepromatous and one was borderline leprosy in reversal reaction. One patient required an emergency tracheostomy and one had an almost complete upper airway obstruction.

Anderson H, Stryjewska B, Boyanton BL, Schwartz MR. Hansen disease in the United States in the 21st century: a review of the literature. *Arch Pathol Lab Med* 2007; 131(6): 982-6.

In this article we review the recent literature on Hansen disease (leprosy). We searched published literature through PubMed (National Library of Medicine) and extracted data through direct review of the literature and pathologic slides. Hansen disease continues to occur in the United States, including among the native-born population. Inclusion of the disease in the differential diagnosis is key to confirmation. Current epidemiology, classification systems, prevention measures, and therapy are reviewed.

Abreu MA, Alchorne MM, Michalany NS, Weckx LL, Pimentel DR, Hirata CH. The oral mucosa in paucibacillary leprosy: a clinical and histopathological study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007; 103(5): 48-52.

BACKGROUND: Involvement of the oral mucosa can occur in lepromatous leprosy; however, lesions in the oral mucosa of paucibacillary patients have not been previously observed. **OBJECTIVE:** The objective of this study is to determine whether clinical and subclinical lesions exist in oral mucosa in nontreated paucibacillary leprosy patients, using clinical and histopathological examination. **MATERIALS AND METHODS:** A clinical and histopathological study involving 30 untreated paucibacillary leprosy patients was conducted. All patients underwent biopsies of the buccal mucosa, soft palate, and tongue. When acid-fast bacilli in association with inflammatory infiltrate, granulomatous or not, were encountered, it was considered [quot]specific[quot] involvement of the oral mucosa; and [quot]nonspecific[quot] involvement when the bacilli were not encountered. **RESULTS:** Eight nonspecific chronic inflammatory reactions and 1 granulomatous inflammatory process without acid-fast bacilli were detected. **CONCLUSIONS:** Paucibacillary leprosy patients do not exhibit specific, clinical or subclinical, involvement in the oral mucosa; nonspecific alterations occur even in the absence of signs and symptoms.

Iyer AM, Mohanty KK, Egmond D, Katoch K, Faber WR, Das PK, Sengupta U. Leprosy-specific B-cells within cellular infiltrates in active leprosy lesions. *Hum Pathol*; 38(7): 1065-73.

Leprosy is a spectral disease with polar lepromatous and tuberculoid forms correlating with enhanced humoral and cell-mediated immunity, respectively, against *Mycobacterium leprae* and the borderline forms, borderline lepromatous, midborderline, and borderline tuberculoid showing in-between clinical and immunological characteristics. Histopathologically, the cellular infiltrates of leprosy lesions show predominantly the presence of interacting T-cells and antigen presenting cells like macrophages, whereas the presence of B-cells has only been sporadically reported. The present study demonstrates by immunohistochemical techniques the presence of B-cells, including plasma cells, in active lesions from lepromatous leprosy, skin smear negative borderline lepromatous, and paucibacillary borderline tuberculoid leprosy. Furthermore, the study demonstrates the in situ production of *M leprae*-specific antibodies from BT lesions using an organotypic skin explant culture model. Finally, analysis of the cytokine release profile in supernatants of lesional organotypic skin cultures showed a microenvironment conducive to the differentiation and maturation of B-cells. The results demonstrate the presence of different functionally active B-cell stages within lesions of patients with leprosy, including borderline tuberculoid patients, which could secrete anti-*M leprae*-specific antibodies. However, their role in leprosy pathology remains to be elucidated.

PREVENÇÃO

Zodpey SP. Protective effect of bacillus Calmette Guerin (BCG) vaccine in the prevention of leprosy: a meta-analysis. *Indian J Dermatol Venereol Leprol* 2007; 73(2): 86-93.

BACKGROUND: Although the role of bacillus Calmette Guerin (BCG) vaccine in the prevention of leprosy was hypothesized as early as 1939, its level of protective effect remained controversial. **AIM:** As a meta-analysis systematically combines the results from different studies, we summarize the protective effect of BCG vaccine in prevention of leprosy using meta-analytic procedures. **METHODS:** Our search strategy included a computerized literature search, snowballing technique to identify potential studies, review of previously compiled lists of BCG studies and articles, contacting experts on BCG vaccination and manual search to locate articles in non-indexed journals. The present meta-analysis included 22 studies (6 trials, 2 cohort studies and 14 case-control studies) on the role of BCG vaccine in the prevention of leprosy. The random effects model as described by DerSimonian and Laird was used to summarize the effect measures. For each summarization, a Chi-square test of heterogeneity was estimated. To strengthen the viewpoint further additional information from the studies which were not included in meta-analysis, was also utilized. **RESULTS:** The summary protective effects calculated from trials, cohort studies and case-control studies were 43 (27-55), 62 (53-69) and 58 (47-67)% respectively, which were statistically significant. These estimates confirmed the protective association between BCG vaccination and leprosy. Review of 29 studies focusing on the role of BCG vaccination in the prevention of leprosy revealed that not a single study reported a negative protective effect. Thirteen (44.8%) studies demonstrated greater than or equal to 50% efficacy/effectiveness. **CONCLUSION:** There is sufficient and convincing evidence of the protective effect of BCG vaccine against leprosy, as reflected from the meta-analysis and overall review of 29 studies of BCG vaccination and leprosy.

Greco DB, Simão M. Brazilian policy of universal access to AIDS treatment: sustainability challenges and perspectives. *AIDS* 2007; 21 Suppl 4: S37-45.

INTRODUCTION: The Brazilian AIDS Programme success is recognized worldwide, due to its integrated approach of prevention, respect for human rights and to free of charge universal access to state of the art antiretrovirals. **CURRENT SITUATION:** As of 2006, 180,000 people living with AIDS are on HAART with 17 drugs available, receiving medical and laboratory care through the public health system. Costs for ART drugs reached US\$ 400 million in 2006 and will increase steeply if the current trends are maintained: uptake of approximately 20,000 new patients/year and the need for more expensive, patent-protected second and third line drugs. **DISCUSSION:** We discuss the strengths and weaknesses of the programme, budgetary pressures, the need for more intense preventive efforts, for boosting local production of new drugs, for more investment in research and development and the issue of voluntary and compulsory licensing. There are many hurdles in pursuing long-term sustainability, which depends on country driven initiatives and international collaboration and participation. **CONCLUSION:** We conclude that the Brazilian experience demonstrated the capability of a developing country to treat people with equity, independently of race, gender or economic power and that this equality [quot] has already spread to other countries. Internally this experience must be used to tackle other endemic diseases, such as leprosy, malaria, dengue and leishmania. The Brazilian political will has been proven but, once again, there will be the need for concerted action by civil society, researchers, health professionals, people living with HIV/AIDS and the government to convince the world that health needs should not be treated as commercial issues, and that progress in research and development must be shared throughout the world if we expect to survive as a civilization.

Velema JP, Ogbeiwi OI. ILEP organisations should strive for high BCG coverage in communities at risk of leprosy. *Lepr Rev* 2007; 78(2): 88-101.

The central thesis of this paper is that the EPI policy of a BCG vaccination at birth or in the first year of life provides proven partial protection against leprosy and that ILEP organisations should actively encourage government health services to maintain a high coverage. A literature review identified 12 case-control studies showing a median vaccine efficacy of 63% (range 20-90%). Two prospective studies and two randomised community trials showed a median efficacy of 70% (range 42-80%). The duration of this partial protection is at least 10-15 years. Studies of the long-term protective effect of BCG vaccination against leprosy have not been conducted. One trial has demonstrated a reduction of tuberculosis incidence up to 40 years after vaccination with BCG. There is a growing consensus that BCG works by 'upgrading' the immune response to *M. leprae*, moving leprosy cases from the lepromatous end of the Ridley-Jopling classification to the tuberculoid end or even makes it possible for infection to remain subclinical. An analysis of national BCG coverage figures as reported to WHO showed that the global mean coverage increased from 58% in 1980 to 88% in 2003. The absolute number of countries reporting less than 80% coverage has decreased from 78 out of 105 in 1981 to 32 of 157 in 2003. Only four countries reported coverages below 60% in 2003. Twenty of the 53 African countries reported coverages below 80% in 2003 against five of 38 countries in Asia, five of 13 countries in Oceania and two of 27 in Central and South America. Comparison of officially reported national coverage to estimates of coverage from special surveys clearly shows that the national figure may not adequately reflect the local situation. Rural communities often have lower coverage than urban populations. Slum households have lower coverage than non-slum households. Remote areas may not be touched by modern health services. Pockets of low BCG coverage exist in countries where leprosy is endemic and ILEP organisations are active. ILEP organisations can make an impact, not

by getting involved in vaccination work directly, but by monitoring the BCG coverage and advocating for adequate provision of MCH services in the communities in which they work. This will reduce the risk of leprosy in children up to 15 years of age, provide a number of other benefits to the mothers and children involved and potentially contribute to a reduction of leprosy incidence on the longer term. If the partial protection imparted by BCG is life-long, adding a consistently high BCG coverage to the usual strategy of early case detection and treatment could result in a halving of the leprosy incidence in 2020.

PSICOLOGIA

Tsutsumi A, Izutsu T, Islam AM, Maksuda NA, Kato H, Wakai S. The quality of life, mental health, and perceived stigma of leprosy patients in Bangladesh. *Soc Sci Med* 2007; 64(12): 2443-53.

Resumo: The present study aims to determine the quality of life (QOL) and general mental health of leprosy patients compared with the general population, and evaluate contributing factors such as socio-economic characteristics and perceived stigma. A total of 189 patients (160 outpatients, 29 inpatients) and 200 controls without leprosy or other chronic diseases were selected from Dhaka district, Bangladesh, using stratified random sampling. A Bangladeshi version of a structured questionnaire including socio-demographic characteristics-the Bangla version of the World Health Organization Quality of Life Assessment BREF (WHOQOL-BREF)-was used to assess QOL; a Self-Reporting Questionnaire (SRQ) was used to evaluate general mental health; the Barthel Index to control activities of daily living (ADL); and the authors' Perceived Stigma Questionnaire was used to assess perceived stigma of patients with leprosy. Medical records were examined to evaluate disability grades and impairment. QOL and general mental health scores of leprosy patients were worse than those of the general population. Multiple regression analysis revealed that factors potentially contributing to the deteriorated QOL of leprosy patients were the presence of perceived stigma, fewer years of education, the presence of deformities, and a lower annual income. Perceived stigma showed the greatest association with adverse QOL. We conclude that there is an urgent need for interventions sensitive to the effects of perceived stigma, gender, and medical conditions to improve the QOL and mental health of Bangladeshi leprosy patients.

REABILITAÇÃO

Fuzikawa P, Melchior H, Wexler R, Piefer A, Min CS, Rajkumar P, Anderson A, Benbow C, Lehman L, Nicholls P, Saunderson P, Velema JP. The development of a short questionnaire for screening of activity limitation and safety awareness (SALSA) in clients affected by leprosy or diabetes. *Disabil Rehabil* 2007; 29(9): 689-700.

PURPOSE: The purpose of this study was to develop and validate a method of measuring activity limitation in leprosy and diabetes. The resulting questionnaire should be quick and simple to use in basic clinical settings, not require any testing skills or equipment, be validated across a number of cultures in order to be widely applicable, be relevant for anyone with long-standing peripheral neuropathy and be sensitive to changes in clients' capabilities. Because of impaired sensibility in hands or feet, persons affected by leprosy or diabetes are expected to be aware that many activities carry a risk of injury, particularly repetitive stress, excess pressure, friction or burns. They are expected to avoid these risky activities, or modify how they are carried out, in order to prevent injury. An additional aim of the study was therefore to find ways of assessing how far clients were aware of safety issues and how much they limited their activities voluntarily because of safety concerns. METHOD: Lists of activities of daily living relevant for the target populations were generated through individual interviews and focus group discussions. A questionnaire of 374 items was compiled and administered to 436 persons affected by leprosy and 132 affected by diabetes in five countries in four continents. A total of 76% of respondents had impairments. Occupational therapists not otherwise involved in this study gave an independent assessment of the degree of activity limitation of 207 respondents. The process of item selection from this database is presented step by step. Items for the SALSA scale were practised by at least 70% of respondents in all participating populations, were easy to perform for some but difficult for others, correlated well with the assessment of independent practitioners and had good item-total correlation.

The present set of 20 items is well represented by a single principal component and had a high scale reliability coefficient. RESULTS: On a 20-item scale, one would expect a score of 20 if the respondents practiced all the activities listed without difficulty. Higher scores reflect increasing activity limitation. The SALSAs score varied from 10 to 75 with a mean of 32. The distribution of the scores was not different between men and women or between disease groups. There was a consistent increase of the SALSAs score with age and with the level of impairment. Compared to India and Nigeria, the average SALSAs scores, adjusted for age and impairment level, were higher in Israel and Brazil, but lower in China. The spearman correlation coefficient between the SALSAs scores and the scores assigned by the independent experts was 0.67. Among 23 respondents without overt disease, the SALSAs score had a median of 19 and half the respondents scored between 18 and 20. CONCLUSIONS: The present research has resulted in the SALSAs scale, a short questionnaire which can be administered within 10 min and which provides a standardized measure of activity limitation in clients with a peripheral neuropathy. It can be used to make comparisons between (groups of) individuals in different countries and in the same person (or group) over time. General health workers can use SALSAs to screen clients and refer those with high scores to specialised services. In addition, the scale will assist service providers in designing appropriate interventions.

Melchior H, Vatine JJ, Weiss PL. Is there a relationship between light touch-pressure sensation and functional hand ability? *Disabil Rehabil* 2007; 29(7): 567-75.

PURPOSE: To investigate and compare the level of light touch-pressure sensation as tested via the Semmes Weinstein monofilament (SWM) test with the level of functional hand ability. METHODS: Twenty-seven persons with isolated sensory deficit due to leprosy and 31 healthy controls were tested in the Occupational Therapy department of a hospital for patients with Hansen's disease. Palmar light touch thresholds were determined by SMW testing. Functional hand ability was tested via the Jebsen-Taylor Hand Function Test (JTHFT) and the Functional Dexterity Test (FDT). All participants were measured by manual muscle testing (MMT) to exclude any motor impairment. Data analysis compared sensory thresholds and level of functional hand ability between the two groups and examined the relationship between the variables. RESULTS: In the group with sensory deficit, the sensory thresholds were significantly higher than in the control group. Significant correlations were found between the sensory thresholds measured by the SWM test and the FDT and JTHFT scores, with higher correlations found for tasks entailing manipulation of small objects. CONCLUSIONS: The findings support the existence of a relationship between sensory light touch thresholds tested by the Semmes Weinstein monofilaments (SWMs) and hand function. However, the SWM test alone is not sufficient as an indicator of hand function and must therefore be supplemented with other hand function tests.

Literatura corrente em hanseníase

Bauer B, Khoa NK, Chabaud B, Chaise F, Quang HT, Comtet JJ. Transfert tendineux palliatif utilisant le Flexor Superficialis Digitorum dans les paralysies intrinsèques d'origine lépreuse. *Chir Main* 2007; 26(3): 136-40.

A follow up study was performed in the rehabilitation centre for patients with leprosy in Hôchiminhville - Vietnam. All patients had claw-hand deformity due to ulnar and median nerve intrinsic paralysis. Thirty-two affected hands (128 long fingers) were included in the study. A Bunnel-Littler tendon transfer procedure was performed using a four-tailed graft of the flexor digitorum superficialis of the third finger. Clinical evaluation included anatomical measurements of interphalangeal and metacarpal joints in complete extension and in the intrinsic position. In the open hand assessment, 48.5% reported good results, 14.8% medium results and 36.7% poor results. With the hand in the intrinsic position, 53.9% achieved good results, while 33.6% achieved medium results and poor in 12.5%. Poor functional outcome is related to a failure of this procedure and seems to be due to extensor tendon laxity, with or without stiffness of the interphalangeal joints. There were many anatomical deformities (27.3%) found at the time of follow up, notably boutonniere (51.4%) and mallet finger deformities (31.4%) The fourth and fifth fingers had the worst results. We have therefore decided to change our protocol for claw-hand correction and use the Bouvier test in deciding on our surgical indications. Preoperative physiotherapy is absolutely necessary to reduce stiffness of the interphalangeal joints.

TERAPÊUTICA

Wang F, Langley R, Gulten G, Dover LG, Besra GS, Jacobs WR, Sacchettini JC. Mechanism of thioamide drug action against tuberculosis and leprosy. *J Exp Med* 2007; 204(1): 73-8.

Thioamide drugs, ethionamide (ETH) and prothionamide (PTH), are clinically effective in the treatment of *Mycobacterium tuberculosis*, *M. leprae*, and *M. avium* complex infections. Although generally considered second-line drugs for tuberculosis, their use has increased considerably as the number of multidrug resistant and extensively drug resistant tuberculosis cases continues to rise. Despite the widespread use of thioamide drugs to treat tuberculosis and leprosy, their precise mechanisms of action remain unknown. Using a cell-based activation method, we now have definitive evidence that both thioamides form covalent adducts with nicotinamide adenine dinucleotide (NAD) and that these adducts are tight-binding inhibitors of *M. tuberculosis* and *M. leprae* InhA. The crystal structures of the inhibited *M. leprae* and *M. tuberculosis* InhA complexes provide the molecular details of target-drug interactions. The purified ETH-NAD and PTH-NAD adducts both showed nanomolar K_{is} against *M. tuberculosis* and *M. leprae* InhA. Knowledge of the precise structures and mechanisms of action of these drugs provides insights into designing new drugs that can overcome drug resistance.

Walker SL, Lockwood DN. Leprosy. *Clin Dermatol* 2007; 25(2): 165-72.

Leprosy is a granulomatous disease affecting the skin and nerves caused by *Mycobacterium leprae*. It continues to be a significant public health problem. Despite multidrug therapy, immunologic reactions continue to occur, leading to disability and deformity due to neuropathy. It is important that dermatologists are aware of the neurologic as well as the skin manifestations of the condition so that nerve involvement can be identified and treated rapidly.

Sales AM, Sabroza PC, Nery JÁ, Duppre NC, Sarno EM. No difference in leprosy treatment outcomes comparing 12- and 24-dose multidrug regimens: a preliminary study. *Cad Saude Publica* 2007; 23(4): 815-22.

Resumo: A comparative study was performed on the initial and final bacillary indexes of 213 multibacillary leprosy patients who received 12 doses (Group 1: 128 patients) or 24 doses (Group 2: 85 patients) of multidrug therapy (MDT/WHO) to measure the effectiveness of the two regimens. All patients were evaluated at treatment baseline, 12 months, and 24 months. The reduction in bacillary levels and mean bacillary indexes at 24 months was similar in the two groups. No statistical difference in reaction rates was observed between the two treatment regimens.

Maslov AK, Khivrina AS. [Prospects for leprosy treatment via complexation of rifampicin with iodide and horse-radish root]. *Probl Tuberk Bolezn Legk*; (4): 25-7.

A model of leprosy was used to study the therapeutic effect of horse-radish root (HRR) containing peroxidase in combination with rifampicin (RFP) and potassium iodide (PI) as compared to routine combined therapy with RFP and diaminodiphenylsulfonum. Therapy with HRR and iodide showed the best antimicrobial effect than the routine combined therapy. A combination of RFP, HRR, and PI increased the activity of neutrophilic myeloperoxidase produced an anti-inflammatory activity and caused no persistent anemia or toxic effect on the murine liver.

Andersson AK, Atkinson SE, Khanolkar-Young S, Chaduvula M, Jain S, Suneetha L, Suneetha S, Lockwood DN. Alteration of the cortisol-cortisone shuttle in leprosy type 1 reactions in leprosy patients in Hyderabad, India. *Immunol Lett* 2007; 109(1): 72-5.

Regulation of inflammation in leprosy may be influenced by local concentrations of active cortisol and inactive cortisone, whose concentrations are regulated by enzymes in the cortisol-cortisone shuttle. We investigated the cortisol-cortisone shuttle enzymes in the skin of leprosy patients with type 1 reactions (T1R), which are characterised by skin and nerve inflammation. Gene expression of the shuttle enzymes were quantified in skin biopsies from 15 leprosy patients with new T1R before and during prednisolone treatment and compared with levels in skin biopsies from 10 borderline leprosy patients without reactions. Gene expression of 11beta-hydroxysteroid dehydrogenase (11beta-HSD) type 2, which converts cortisol to cortisone, is down-regulated in skin from T1R lesions. However expression levels of 11beta-HSD type 1, which converts cortisone to cortisol, were similar in skin with and without reactions and did not change during anti-leprosy drug treatment. Prednisolone treatment of patients with reactions is associated with an upregulation of 11beta-HSD2 expression in skin. The down regulation of 11beta-HSD2 at the beginning of a reaction may be caused by pro-inflammatory cytokines in the leprosy reactional lesion and may be a local attempt to down-regulate inflammation. However in leprosy reactions this local response is insufficient and exogenous steroids are required to control inflammation.

Literatura corrente em hanseníase

Van Veen NH, Nicholls PG, Smith WC, Richardus JH. Corticosteroids for treating nerve damage in leprosy. *Cochrane Database Syst Rev* 2007; (2): CD005491

BACKGROUND: Leprosy causes nerve damage which can result in nerve function impairment and disability. Corticosteroids are commonly used for treating nerve damage, although the long-term effect is uncertain. **OBJECTIVES:** To assess the effects of corticosteroids on nerve damage in leprosy. **SEARCH STRATEGY:** We searched the Cochrane Neuromuscular Disease Group Register, the Cochrane Central Register of Controlled Trials (Issue 4), MEDLINE (from 1966), EMBASE (from 1980), CINAHL (from 1980), LILACS (from 1982) in January 2006. We checked reference lists of the studies identified, the Current Controlled Trials Register (www.controlled-trials.com), conference proceedings and contacted trial authors. **SELECTION CRITERIA:** Randomised and quasi-randomised controlled trials of corticosteroids for nerve damage in leprosy. **DATA COLLECTION AND ANALYSIS:** The primary outcome was improvement in sensory and motor nerve function after one year. Secondary outcomes were improvement in nerve function after two years, change in nerve pain and tenderness, and adverse events. Two authors independently extracted data and assessed trial quality. We contacted trial authors for additional information. We collected adverse effects and cost effectiveness information from the trials and non-randomised studies. **MAIN RESULTS:** We included three randomised controlled trials involving 513 people. Two trials compared prednisolone with placebo. One trial treated mild sensory impairment of less than six months duration and the other trial treated nerve function impairment of 6 to 24 months duration. Both trials examined an effect twelve months from the start of treatment. There was no significant difference in nerve function improvement between people treated with prednisolone or with placebo. The third trial compared three corticosteroid regimens for severe type 1 reactions. This trial did not report the prespecified outcomes. However, after 12 months, a significantly higher proportion of individuals on a 3-month course of prednisolone required extra

corticosteroids compared to the groups with a high-dose and low-dose regimen of five months duration. Diabetes and peptic or infected ulcer were sometimes reported as serious adverse events in the placebo-controlled trials, but not significantly more often in the corticosteroid than placebo groups. **AUTHORS' CONCLUSIONS:** Corticosteroids are used for treating acute nerve damage in leprosy, but evidence from randomised controlled trials does not show a significant long-term effect. Randomised controlled trials are needed to establish their effectiveness, the optimal regimens and to examine new therapies.

Booth AV, Kovich OI. Lepromatous leprosy. *Dermatol Online J* 2007; 13(1): 9.

A 51-year-old woman presented with a 2-month history of pruritic, erythematous papules and plaques on her arms that were treated as chronic urticaria. Histopathologic examination demonstrated acid-fast bacilli, and a diagnosis of lepromatous leprosy was made. Presentation and treatment of leprosy are reviewed.

Pandey B, Shrestha K, Lewis J, Hawksworth RA, Walker SL. Mortality due to dapsone hypersensitivity syndrome complicating multi-drug therapy for leprosy in Nepal. *Trop Doct* 2007; 37(3): 162-3.

Dapsone is a component of multi-drug therapy (MDT) for the treatment of all types of leprosy. It is known that dapsone hypersensitivity syndrome (DHS) complicates the treatment in a proportion of patients. We performed a retrospective study of patients commenced on MDT between 1990 and 2006; 2% developed DHS and 0.25% died due to DHS.

Knobloch J, Shaughnessy JD, Rütter U. Thalidomide induces limb deformities by perturbing the Bmp/Dkk1/Wnt signaling pathway. *FASEB J* 2007; 21(7): 1410-21.

Thalidomide, a sedative originally used to treat morning sickness and now used to treat leprosy and multiple myeloma, is also a teratogen that induces birth defects in humans such as limb truncations and microphthalmia. However, the teratogenic mechanism of action of this drug remains obscure. Thalidomide induces limb and eye defects in the chicken embryo at an EC50 of 50 microg/kg egg wt and apoptosis in primary human embryonic fibroblasts (HEFs) at an EC50 of 8.9 microM. Using these model systems, we demonstrate by semiquantitative reverse transcriptase-polymerase chain reaction and whole-mount in situ hybridization that thalidomide-induced oxidative stress enhances signaling through bone morphogenetic proteins (Bmps). This leads to up-regulation of the Bmp target gene and Wnt antagonist Dickkopf1 (Dkk1) with subsequent inhibition of canonical Wnt/beta-catenin signaling and increased cell death as shown by trypan blue and terminal deoxynucleotidyl transferase-mediated nick end labeling staining. Thalidomide-induced cell death was dramatically reduced in HEFs and in embryonic limb buds by the use of inhibitors against Bmps, Dkk1, and Gsk3beta, a beta-catenin antagonist acting downstream of Dkk1 in the Wnt pathway. Most interestingly, blocking of Dkk1 or Gsk3beta dramatically counteracts thalidomide-induced limb truncations and microphthalmia. From this, we conclude that perturbing of Bmp/Dkk1/Wnt signaling is central to the teratogenic effects of thalidomide.

Kar HK, Sharma P. Does concomitant HIV infection have any epidemiological, clinical, immunopathological and therapeutic relevance in leprosy. *Indian J Lepr* 2007; 79(1): 45-60.

Co-infection with HIV-1 and *M. Leprae* is a rare event in endemic areas for leprosy and HIV, such as India. Neither an increased HIV prevalence among leprosy cases, nor any rapid progression to AIDS was observed among dual HIV-leprosy infections. The current situation concerning continued new leprosy case-detection and gradual increase in HIV infection in India and a few other developing countries, such as Brazil, emphasizes the importance of monitoring the occurrence of co-infections. There is so far no change in the clinical spectrum of leprosy, PB/MB ratio, leprosy reactions and neuritis among co-infected patients. All types of leprosy occur in HIV patients [except in one study (Borgdorff et al, 1993) where more MB leprosy cases with HIV infection were seen]. Histopathological observations reveal a normal spectrum of appearance in biopsies of leprosy lesions from co-infected patients suggesting that cell-mediated immune response to *M. Leprae* is preserved at the site of the disease, despite evidence that these responses are abrogated systemically. All dual infection cases respond to regular treatment, except in three studies which noted more relapses. Therefore, a longer duration of surveillance is advisable after fixed duration therapy, for the detection of early relapse. Type 2 reaction can be managed with a higher dose of clofazimine. Type 1 reaction when developed as such, or as IRIS, needs oral steroids in adequate doses, particularly when associated with neuritis and motor loss, since lower doses may not be able to reverse the motor loss even of early onset. However, higher doses of corticosteroid when given need to be monitored closely. The impact of immune restoration in co-infected patients receiving ART is commonly observed in cases with borderline leprosy.

